USDA-APHIS Biotechnology Regulatory Services
User's Guide

Notification

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

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The information contained in this document is intended solely as guidance, and reflects APHIS' current interpretation of applicable statues and regulations. 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. Throughout the document, sections from applicable statutes and regulations are clearly identified in grey-shaded text boxes.

Conversely, following the guidelines contained in this document should not be construed as a guarantee of compliance with applicable statutes and regulations.

Notification

Quick Guide to Notification

Notification is an administratively streamlined alternative to the permit process to allow the introduction of a certain subset of genetically engineered plants.

- The goal of the notification procedure is the same as the permit system: *preventing the unintended release of the regulated article*.
- Introductions of genetically engineered *plants* may use the notification procedure if:
    - The introduced plant meets **all** of six eligibility criteria (p. 7) AND,
    - The introduction (the importation, interstate movement, or environmental release) will meet **all** of six performance standards (p. 10).
    - Design protocols articulate how the applicant intends to meet the required performance standards (p. 20).
- By submitting a notification to APHIS, the applicant certifies to APHIS that the introduction will meet both specified eligibility criteria and performance standards.
    - The submission document contains information that helps APHIS determine the appropriateness of the notification process for the proposed introduction (p. 16).
    - Notification should be submitted to APHIS:
        - At least 10 days prior to an interstate movement of a regulated article, or
        - At least 30 days prior to an importation or environmental release of a regulated article
- APHIS sends copies of the notification to state regulatory officials for review in each state where the introduction has been proposed (p. 22).
- If APHIS agrees that the introduction meets eligibility criteria and performance standards, APHIS will send a letter of acknowledgement to the applicant:
    - Within 10 days of receipt of a notification of interstate movement, or
    - Within 30 days of receipt of a notification of importation or environmental release.
- Introductions *may not proceed* without a letter of acknowledgement from APHIS.
- Applicants must promptly notify APHIS of any unusual occurrences that happen during the introduction (p. 25).
- All introductions are subject to inspection by federal and/or state inspectors (p. 26).
- A field test report must be submitted to APHIS within 6 months of the termination of an environmental release (p. 28).

The notification procedure is explained in 7 C.F.R. 340.3:

"Sec. 340.3 Notification for the introduction of certain regulated article.[5]

(a) General. Certain regulated articles may be introduced without a permit, provided that the introduction is in compliance with the requirements of this section. Any other introduction of regulated articles require a permit under Sec. 340.4, with the exception of introductions that are conditionally exempt from permit requirements under Sec. 340.2(b) of this part.

(b) Regulated articles eligible for introduction under the notification procedure. Regulated articles which meet all of the following six requirements and the performance standards set forth in paragraph (c) of this section are eligible for introduction under the notification procedure.

(1) The regulated article is any plant species that is not listed as a noxious weed in regulations at 7 CFR part 360 under the Plant Protection Act (7 U.S.C. 7712), and, when being considered for release into the environment, the regulated article is not considered by the Administrator to be a weed in the area of release into the environment.

(2) The introduced genetic material is ``stably integrated'' in the plant genome, as defined in Sec. 340.1.

(3) The function of the introduced genetic material is known and its expression in the regulated article does not result in plant disease.

(4) The introduced genetic material does not:

(i) Cause the production of an infectious entity, or

(ii) Encode substances that are known or likely to be toxic to nontarget organisms known or likely to feed or live on the plant species, or

(iii) Encode products intended for pharmaceutical or industrial use.

(5) To ensure that the introduced genetic sequences do not pose a significant risk of the creation of any new plant virus, plant virus-derived sequences must be:

(i) Noncoding regulatory sequences of known function, or

(ii) Sense or antisense genetic constructs derived from viral genes from plant viruses that are prevalent and endemic in the area where the introduction will occur and that infect plants of the same host species, and that do not encode a functional noncapsid gene product responsible for cell-to-cell movement of the virus.

(6) The plant has not been modified to contain the following genetic material from animal or human pathogens:

(i) Any nucleic acid sequence derived from an animal or human virus, or

(ii) Coding sequences whose products are known or likely causal agents of disease in animals or humans.

(c) Performance standards for introductions under the notification procedure. The following performance standards must be met for any introductions under the notification procedure.

(1) If the plants or plant materials are shipped, they must be shipped in such a way that the viable plant material is unlikely to be disseminated while in transit and must be maintained at the destination facility in such a way that there is no release into the environment.

(2) When the introduction is an environmental release, the regulated article must be planted in such a way that they are not inadvertently mixed with non-regulated plant materials of any species which are not part of the environmental release.

[5]APHIS may issue guidelines regarding scientific procedures, practices, or protocols which it has found acceptable in making various determinations under the regulations. A person may follow an APHIS guideline or follow different procedures, practices, or protocols. When different procedures, practices, or protocols are followed, a person may, but is not required to, discuss the matter in advance with APHIS to help ensure that the procedures, practices, or protocols to be followed will be acceptable to APHIS."

Sec. 340.3 Notification for the introduction of certain regulated article (cont'd)

(c) *continued…*

"(3) The plants and plant parts must be maintained in such a way that the identity of all material is known while it is in use, and the plant parts must be contained or devitalized when no longer in use.

(4) There must be no viable vector agent associated with the regulated article.

(5) The field trial must be conducted such that:

(i) The regulated article will not persist in the environment, and

(ii) No offspring can be produced that could persist in the environment.

(6) Upon termination of the field test:

(i) No viable material shall remain which is likely to volunteer in subsequent seasons, or

(ii) Volunteers shall be managed to prevent persistence in the environment.

(d) Procedural requirements for notifying APHIS. The following procedures shall be followed for any introductions under the notification procedure:

(1) Notification should be directed to the Animal and Plant Health Inspection Service, Plant Protection and Quarantine, Biotechnology and Scientific Services, Biotechnology Permits, 4700 River Road, Unit 147, Riverdale, Maryland 20737-1237.

(2) The notification shall include the following:

(i) Name, title, address, telephone number, and signature of the responsible person;

(ii) Information necessary to identify the regulated article(s), including:

(A) The scientific, common, or trade names, and phenotype of regulated article,

(B) The designations for the genetic loci, the encoded proteins or functions, and donor organisms for all genes from which introduced genetic material was derived, and

(C) The method by which the recipient was transformed;

(iii) The names and locations of the origination and destination facilities for movement or the field site location for the environmental release; and the size of the introduction,

(iv) The date and, in the case of environmental release, the expected duration of the introduction (release); and

(v) A statement that certifies that introduction of the regulated article will be in accordance with the provisions of this section.

(3) Notification must be submitted to APHIS:

(i) At least 10 days prior to the day of introduction, if the introduction is interstate movement.

(ii) At least 30 days prior to the day of introduction, if the introduction is an importation.

(iii) At least 30 days prior to the day of introduction, if the introduction is an environmental release.

(4) Field test reports must be submitted to APHIS within 6 months after termination of the field test. Field test reports shall include the APHIS reference number, methods of observation, resulting data, and analysis regarding all deleterious effects on plants, nontarget organisms, or the environment.

(5) The Administrator, shall be notified of any unusual occurrence within the time periods and in the manner specified in Sec. 340.4(f)(10).

(6) Access shall be allowed for APHIS and State regulatory officials to inspect facilities and/or the field test site and any records necessary to evaluate compliance with the provisions of paragraphs (b) and (c) of this section.

(e) Administrative action in response to notification.

(1) APHIS will provide copies of all notifications to appropriate State regulatory official(s) for review within 5 business days of receipt. Comments to APHIS from appropriate State regulatory officials in response to notifications for interstate movement of regulated articles will not be required by APHIS prior to acknowledgment, although States may provide their reviews to APHIS at their discretion.

Sec. 340.3 Notification for the introduction of certain regulated article (cont'd)

(e) *continued…*

(2) The Administrator, will provide acknowledgement within 10 days of receipt that the interstate movement is appropriate under notification.

(3) The Administrator, will provide acknowledgement within 30 days of receipt that the importation is appropriate under notification.

(4) APHIS will provide acknowledgment within 30 days of receipt that the environmental release is appropriate under notification. Such acknowledgment will apply to field testing for 1 year from the date of introduction, and may be renewed annually by submission of an additional notification to APHIS.

(5) A person denied permission for introduction of a regulated article under notification may apply for a permit for introduction of that regulated article without prejudice."

Notification for the Introduction of Certain Regulated Articles

Notification is an alternative to the permit process for the introduction (interstate movement, importation, or environmental release) of certain genetically engineered plants that are regulated articles. Importation means moving regulated articles from a foreign country into the United States; whereas, interstate movement means moving the regulated articles from one U.S. State to another. To make use of the notification procedure, you must be introducing a plant species that meets all of six eligibility criteria, and you must introduce it in accordance with specified performance standards.

> ***Introduce or introduction:*** To move into or through the United States, to release into the environment, to move interstate, or any attempt thereat (§ 340.1).

A notification is a document sent to APHIS from the party who plans to introduce a regulated article, which certifies that the introduction will meet the required eligibility and performance standards. APHIS reviews the notification for appropriateness of the proposed introduction under the notification process. If APHIS agrees that the introduction does not require a permit, APHIS will acknowledge receipt of the notification within 10-30 days, depending upon the type of introduction. Introductions *may not proceed* without a letter of acknowledgement from APHIS.

Notification is an administratively streamlined procedure to facilitate introductions of regulated articles with which APHIS has a great deal of familiarity. This familiarity gives APHIS confidence that the regulated article will not be released beyond the proposed introduction (both in time and space) if the responsible party certifies that specified criteria will be met. However, the ultimate goal of both the notification and permit systems is identical: *preventing the unintended release of the regulated article*.

Most applicants who wish to introduce regulated articles use the notification procedure. In 2005, APHIS acknowledged 1313 introductions under the notification process; in the same period, APHIS granted 97 permits.

Please note that other Federal and State plant quarantine laws may restrict or prohibit the interstate movement, importation, or release of the regulated article. Further, although a pathogen-resistant plant variety may be eligible for introduction under the notification procedure, introduction of the *pathogen* may still require additional permits (e.g. challenge-inoculation experiments of resistant plants). It is the applicant's responsibility to obtain any additional permits required by Federal and State law. For more information on Federal quarantine laws, visit APHIS Plant Protection and Quarantine: http://www.aphis.usda.gov/ppq/index.html. The National Plant Board provides information about State-level quarantine laws: http://nationalplantboard.org/laws/index.html.

History of the Notification Process
Beginning with the Coordinated Framework in 1986, APHIS oversaw introductions of regulated articles by granting permits. In 1993 APHIS introduced the notification procedure as a streamlined alternative to permitting for crops with which APHIS had developed familiarity. At first, notifications were limited to six crops: corn, cotton, potato, soybean, tobacco, and tomato. In 1997 APHIS expanded the notification process to include many other plant species.

Qualifying for the Notification Process

Only introductions of genetically engineered *plants* are eligible for the notification process. Genetically engineered insects, nematodes, bacteria, viruses and other regulated organisms do not qualify for notification; a permit application must be submitted for introductions of these organisms. Further, because the duration of a release under notification is limited to one year, environmental releases of most perennial and biennial plant species must be authorized under a permit, unless the release will be fully terminated within one year.

To qualify for the notification process, the applicant must certify that: 1) the regulated article meets specific **Eligibility Criteria**; and 2) the introduction will meet specified **Performance Standards**. If the regulated article does not meet all of the eligibility requirements or all of the performance standards cannot be met, the introduction may still be allowed under a permit. Eligibility criteria and performance standards for notifications are outlined below.

Eligibility Criteria

In order to introduce a regulated article under the notification procedure, the regulated article must meet all of the six eligibility criteria described below. Eligibility criteria are characteristics of the regulated article (i.e. the plant) and the introduced genetic material.

If you have questions about whether a proposed introduction will meet all six eligibility criteria, contact APHIS as far in advance of the proposed introduction as possible. Introductions that do not meet all six eligibility criteria may still be eligible for introduction under a permit, but the approval of a permit may take longer than notification.

The eligibility criteria are:

1. Recipient organism is not listed as a noxious weed nor considered by APHIS to be a weed in the area of release

"The regulated article is any plant species that is not listed as a noxious weed in regulations at 7 CFR part 360 under the Plant Protection Act (7 U.S.C. 7712), and, when being considered for release into the environment, the regulated article is not considered by the Administrator to be a weed in the area of release into the environment." (§ 340.3(b)(1))

Most common crops meet this eligibility criterion. Plant species listed as noxious weeds in 7CFR360 are not eligible for notification. Additionally, if the plant species may be *considered* a weed in the area of release—a judgment made by the APHIS Administrator, usually in

collaboration with state agricultural officials— the introduction will not be eligible for notification.

Note that the 'considered to be a weed' clause only applies to notifications of release into the environment, and *not* notifications of importation or interstate movement. If there is any question that the engineered plant could be considered a weed in the area of release, contact APHIS as far in advance of the proposed introduction as possible.

2. Stable integration of genetic material

> "The introduced genetic material is 'stably integrated' in the plant genome, as defined in Sec. 340.1." (§ 340.3(b)(2))

> **Stably Integrated.** The cloned genetic material is contiguous with elements of the recipient genome and is replicated exclusively by mechanisms used by recipient genomic DNA (§ 340.1).

The DNA may be inserted into any part of the genome of the plant including nuclear, mitochondrial or chloroplast genomes. The method of transformation must result in a stable integration. Vectors that can mobilize or replicate naturally would not be considered to be a stable transformation. Crosses designed to mobilize, alter or replicate (i.e. increase copy number) stably inserted cloned genetic material are not eligible for notification. However, field experiments using these constructs in their stable form do meet this eligibility requirement.

3. Known function of genetic material that does not result in plant disease

> "The function of the introduced genetic material is known and its expression in the regulated article does not result in plant disease." (§ 340.3(b)(3))

The intent of this criterion is to exclude the use of introduced genetic material that would result in plant disease. This criterion excludes many sequences expressing pathogenesis-related proteins. This also requires that the applicant knows enough about the function of the genetic material to assert that it does not cause plant disease.

To make the assertion that an inserted sequence is unlikely to result in plant disease, the function of the inserted material in the plant must have been determined by empirical observation, or inferred from a high degree of sequence similarity to sequences with an empirically determined function. This criterion excludes, for example, nucleotide sequences whose sole identification or characterization is based upon expression in response to a particular chemical or physical stimulus. The criterion also excludes experiments in which random clones of unknown function have been inserted (e.g. cosmid or cDNA library screening experiments).

4. Characteristics of gene and gene product

> "The introduced genetic material does not: (i) Cause the production of an infectious entity, or (ii) Encode substances that are known or likely to be toxic to nontarget organisms known or likely to feed or live on the plant species, or (iii) Encode products intended for pharmaceutical or industrial use." (**§** 340.3(b)(4))

This criterion has three components. The first ensures that the plant has not been modified to produce an infectious entity, such as a plant virus, an animal virus, a human virus, or other infectious entities. This criterion does *not* exclude use of genetic materials from infectious entities per se, so long as a complete infectious entity cannot be produced.

The second component prevents introductions of plants that are likely to be toxic to organisms living or feeding on the plants. Plants that are designed to be toxic to some organisms— the 'target organisms'—are *not* excluded (for example, plants producing *Bt* toxins). This also allows the introduction of plants that may be toxic to nontarget organisms that are *not* likely to feed or live on the introduced plant, i.e. organisms that are not associated with the plant during the field trial.

Finally, the plant must not express compounds intended for pharmaceutical or industrial use. These plants always require a permit.

Plants are considered to express compounds intended for pharmaceutical use if commercialization of the compound would require approval of one of the following agencies:

(1) FDA's Center for Biologics Evaluation and Research (human biologics);
(2) FDA's Center for Drug Evaluation and Research (human drugs);
(3) FDA's Center for Veterinary Medicine (animal drugs); or
(4) USDA's Center for Veterinary Biologics (animal biologics).

Plants that meet the following three criteria are considered to produce industrial compounds:

(1) The plants are engineered to produce compounds that are new to the plant;
(2) The new compound has not been commonly used in food or feed; and
(3) The new compound is being expressed for non-food, non-feed industrial uses. Industrial uses include, but are not limited to, detergent manufacturing, paper production, and mineral recovery.

Plants engineered for *tolerance* to heavy metals and which are to be used in agricultural production are not excluded from the notification process by this criterion. However, plants that *accumulate* or *detoxify* soil contaminants and are not intended for food or feed use require a permit.

5. Does not pose significant risk of creating new plant viruses.

> "To ensure that the introduced genetic sequences do not pose a significant risk of the creation of any new plant virus, plant virus-derived sequences must be: (i) Noncoding regulatory sequences of known function, or (ii) Sense or antisense genetic constructs derived from viral genes from plant viruses that are prevalent and endemic in the area where the introduction will occur and that infect plants of the same host species, and that do not encode a functional noncapsid gene product responsible for cell-to-cell movement of the virus." (§ 340.3(b)(5))

The intent of this criterion is to prevent the creation of new plant viruses that might result from recombination of the introduced genetic material with genetic material from endemic viruses. Introduced sequences derived from plant viruses must be *either* noncoding sequence *or* sequences that are 1) from viruses prevalent and endemic in the same plant species in the proposed area of introduction and 2) do not encode a functional cell-to-cell movement protein. Eligible non-coding sequences include promoters, enhancers, introns with enhancer activity, upstream activating sequences, polyadenylation signals, transcription terminators, or other known regulatory sequences. In addition to anti-sense constructs, eligible constructs also include those using other mechanisms of RNA-mediated gene silencing of virus genes.

6. Does not contain sequences from human or animal pathogens

> "The plant has not been modified to contain the following genetic material from animal or human pathogens: (i) Any nucleic acid sequence derived from an animal or human virus, or (ii) Coding sequences whose products are known or likely causal agents of disease in animals or humans." (§ 340.3(b)(6))

Plants containing any nucleic acid sequence derived from an animal or human virus are not eligible for notification (*e.g.*, hemagglutinin components derived from human influenza virus). In addition, plants containing coding sequences whose products are known or likely causal agents of disease in humans or nontarget animals are not eligible (*e.g.*, expression of cholera toxin A). Under a separate statutory authority, APHIS cannot acknowledge notifications involving select agents, genes from select agents, or toxins produced by select agents. For more information on select agents, visit: http://www.aphis.usda.gov/programs/ag_selectagent/index.html

Performance Standards

The performance standards are a set of six conditions that must be met in order to ensure that the regulated article is introduced in such a way that it is not inadvertently released beyond the proposed introduction, allowing it to persist in the environment. Generally, performance standards are characteristics associated with the act of introduction (importation, interstate movement, or environmental release).

The goal of performance standards is to manage the introduced regulated article such that it or its offspring are unlikely to persist in the environment. The applicant is given flexibility in developing protocols appropriate to the introduction. However, in the notification the applicant *certifies* that the performance standards will be met (see **Information to Include in a**

Notification: 9. Certification below), and is legally responsible for meeting those standards regardless of the methods selected.

If you have questions about whether a proposed introduction will meet all six performance standards, please contact APHIS before beginning the notification process. Applicants are encouraged to discuss with APHIS any relevant biological considerations associated with particular plant species that may affect the ability to meet performance standards.

Introductions that do not meet all six eligibility criteria may still be eligible for introduction under a permit. Additionally, the guidelines for environmental releases under permit, described in other guidance documents, may be helpful in meeting the performance standards for notifications.

The required performance standards are:

1. Shipping and maintenance at destination

> "If the plants or plant materials are shipped, they must be shipped in such a way that the viable plant material is unlikely to be disseminated while in transit and must be maintained at the destination facility in such a way that there is no release into the environment." (**§** 340.3(c)(1))

Plant materials shipped under the notification procedure must be packaged to ensure that plant material is unlikely to be released from the shipping container in transit. The shipping container requirements described in 7 CFR 340.8 or similar shipping methods are sufficient to meet this performance standard. However, note that movements under notification are *not* required to follow the container regulations in 7 CFR 340.8.

APHIS does not regulate the use of transgenic organisms in contained facilities, and does not evaluate the adequacy of research and storage facilities to prevent release into the environment. However, unauthorized releases of transgenic material from such facilities are a violation of APHIS regulation. APHIS strongly encourages applicants to ensure that destination facilities follow containment guidelines established by the National Institutes of Health or other similar protocols.

For more information about contained facilities, see:

- *Guidelines for Research Involving Recombinant DNA Molecules* (National Institutes of Health): http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html
- *Practical Guide to Containment— Greenhouse Research with Transgenic Plants and Microbes* (Information Systems in Biotechnology, Virginia Tech): http://www.isb.vt.edu/cfdocs/greenhouse_manual.cfm

2. Inadvertent mixing of materials in environmental releases.

> "When the introduction is an environmental release, the regulated article must be planted in such a way that they are not inadvertently mixed with non-regulated plant materials of any species which are not part of the environmental release." (**§** 340.3(c)(2))

Inadvertent mixing of regulated material and nonregulated material can usually be prevented by planting the regulated article in a defined area with an unplanted alley or other easily distinguishable zone between it and any other material. These areas should not be planted with a species that will be harvested or that is sexually compatible with the regulated article. Alleys between the transgenic field plot and neighboring plots should be sufficient to allow movement of planting and harvesting equipment and other farm implements in such a way that seed or vegetative propagules do not become deposited outside of the transgenic field test site and mixed with plant species that are not part of the field trial. Farm implements that can retain viable seed or other propagules should be cleaned on the transgenic field test site or otherwise treated to meet the performance standards. Persons granted access to the test site should be made aware of any protocols used to meet the performance standards, to ensure that their actions at the site will be consistent with those requirements.

This performance standard is also intended to prevent pollination of sexually compatible crops that may be within pollination distance of the field trial. The issue of pollen movement is discussed more fully under Performance Standard 5.

3. Maintaining identity and devitalization.

> "The plants and plant parts must be maintained in such a way that the identity of all material is known while it is in use, and the plant parts must be contained or devitalized when no longer in use." (**§** 340.3(c)(3))

This performance standard ensures that the regulated articles are clearly identified at all times so that they are not inadvertently confused with other plant materials, and to ensure that they are either destroyed or contained after the duration of the introduction.

Identity of transgenic materials may be maintained with adequate labeling, record keeping, and by planting transgenic plants in distinct plots. See also Performance Standard 2 for more guidelines on preserving the identity of regulated material in the field.

Methods of final disposition and devitalization might include:

- Harvest of all seed, ears, tubers, or other reproductive material for transport to devitalization or containment facilities
- Incorporation of all remaining vegetative material at the test site into the soil for decomposition or above-ground composting
- Treatment of the remaining vegetative material with an appropriate registered herbicide

- In the case of woody perennial species, trees, and vines, removal of the plants to a contained facility or cutting and mulching, chipping or exposing the plants to high temperature treatment (i.e., autoclaving, oven baking, or incineration, in accordance with local regulations) and ensuring that any underground plant parts capable of reproduction are removed and likewise destroyed.
- For plants allowed to set seed during the field trial, the occurrence and duration of seed dormancy are factors that should also be considered in the design of proper monitoring protocols. For example, some hard seeds may not be destroyed by fumigation.

Plant materials that are not destroyed after the duration of the introduction must be removed to a contained facility to prevent further unauthorized release. The identity of stored seeds and propagative plant parts should continue to be labeled and maintained in such a way that persons handling these materials will know that subsequent introductions require APHIS authorization. See Performance Standard 1 for guidelines on contained facilities.

4. Elimination of viable vector agents.

> "There must be no viable vector agent associated with the regulated article." (**§** 340.3(c)(4))

When the transformation vector agent involved is a live microorganism, such as *Agrobacterium tumefaciens*, the transformed tissue should be free of the bacterium at the time of introduction. Acceptable elimination of the bacterium can be accomplished by treatment of the plant material with appropriate antibiotics.

5. Persistence in the environment.

> "The field trial must be conducted such that: (i) The regulated article will not persist in the environment, and (ii) No offspring can be produced that could persist in the environment." (**§** 340.3(c)(5))

The fifth performance standard is the test that most often determines whether APHIS will allow an introduction under the notification procedure or permit. Plant species having characteristics that make it more likely to persist without human intervention are less likely to be eligible for notification, but may still be eligible for release under a permit.

> **Persistence in the environment.** Producing feral or sustained populations of the regulated article or its offspring that can persist in agricultural or nonagricultural habitats without human intervention. (58 FR 17044,17049).

Introductions of plant species that have "weedy" characteristics may not be able to meet this performance standard. These characters *may* include: abundant seed production and dispersal; seed dormancy or long term seed viability in the soil; reproduction via vegetative structures; rapid population establishment; adaptation for long-distance dispersal (wind, water, animals, etc.); existence of feral populations of non-transgenic plants; individuals found in disturbed habitats.

When the applicant is considering certain crops that contain any of the above characteristics—particularly grasses, trees, and other woody perennials—the applicant should contact BRS and discuss the performance standards before submitting a notification to BRS.

To minimize the likelihood that seed or vegetative propagules are dispersed from an environmental release and create persistent populations, the applicant should consider the following:

- Dispersal mechanisms of seed or vegetative propagation (natural or accidental)
- Whether the site is near waterways or in an area prone to flooding
- Range of possible dispersal
- Likelihood of seed or propagule survival within the range of possible dispersal
- Methods adequate to prevent such dispersal, including appropriate security measures if appropriate
- Ability to monitor for, identify, and destroy any dispersed plants or their progeny

If seeds or propagules are likely to be dispersed long distances (such as by wind or animals), it may be necessary to prevent seed set or to use bagging, netting, or other methods sufficient to prevent dispersal.

If viable pollen may be produced by the regulated plants, the applicant should consider the following:

- Whether the plant is self-pollinating or outcrossing
- The extent and distance of pollen dissemination by wind and/or pollinating insects, birds, or other species, and the occurrence of these species in the area
- The ability of the plant species to produce viable, fertile progeny with sexually compatible wild, weedy, or feral relatives, and their distribution within the range of pollination
- Synchrony of the flowering cycle of the regulated plants with other sexually compatible relatives within the range of pollination
- The ability of hybrid progeny to persist in the environment
- Any precautions that may be taken to minimize pollen movement (such as flower bagging, border rows, male sterility, etc.)
- Any precautions that may be taken to prevent persistence of hybrids in the environment (such as removal or destruction of wild relatives in the area)

In general, the isolation distances for foundation seed production published by the Association of Official Seed Certifying Agencies (AOSCA) should be considered a minimum acceptable distance between the regulated plants and any sexually compatible species. Local seed certification rules may impose greater distances. More stringent methodologies may also be necessary for the applicant to ensure that no progeny will be produced that can persist in the environment.

Isolation distance standards are published in AOSCA's "Yellow Book," which is only available online to members. However, seed isolation distances based upon AOSCA standards for most common crops are published in 7 CFR 201.76, Regulations of the Federal Seed Act.

In most cases, pollen movement from the regulated plants to nearby *cultivated* sexually compatible crop species does not strictly meet the definition of "persistence in the environment," because the resulting hybrid progeny would not reproduce without human intervention. However, hybridization of the regulated article with non-regulated plants *does* violate Performance Standard 2. Therefore, the guidelines in this section to limit pollen movement to wild relatives should also be applied to prevent pollen movement to cultivated relatives.

6. No volunteer plants.

> "Upon termination of the field test: (i) No viable material shall remain which is likely to volunteer in subsequent seasons, or (ii) Volunteers shall be managed to prevent persistence in the environment." (**§** 340.3(c)(6))

Volunteers should be minimized by growing transgenic material in defined areas in the field and by using adequate termination protocols (see Performance Standard 3). The use of stakes, markers, or GPS coordinates to define the area where the transgenic plants were grown may help in identifying volunteers for later elimination. Applicants should have monitoring protocols of adequate duration to ensure that all volunteers have been eliminated by the methods described in the sections above, including those volunteers that may emerge outside of the field plot (e.g. into fallow zones or adjacent fields). See also Performance Standard 5 above.

Procedural Requirements for Notifying APHIS

A notification is a document sent to APHIS from the party introducing the regulated article that certifies that the introduction will meet required eligibility criteria and performance standards. APHIS first reviews the notification for completeness, and then sends copies to appropriate State regulatory officials for review. If the introduction is appropriate for the notification process, APHIS then sends an *acknowledgement letter* to the responsible party named in the notification. Introductions *may not proceed* without a letter of acknowledgement from APHIS.

To notify APHIS of an interstate movement of a regulated article, notification must be submitted *at least ten days prior* to the proposed day of movement. To notify APHIS of an importation or environmental release of a regulated article, notification must be submitted *at least 30 days prior* to the proposed day of importation or release.

> In April 2006, APHIS introduced the *e-Permits* system for electronic submission of notification. Applicants are encouraged to send notification to APHIS electronically using this method. For instructions, visit: http://www.aphis.usda.gov/permits/brs_epermits.shtml

One notification may include multiple plant lines derived from more than one transformation event and/or multiple constructs. However, all lines described in a single notification must be of

the same crop or plant species. If you wish to notify APHIS about introductions of more than one crop species, send separate notifications for each species.

One notification may also include more than one introduction. More specifically, multiple *interstate movements* and/or multiple *environmental releases* (i.e. multiple field trial locations) may be described in the same notification. Notification of interstate movement and of environmental release may be combined in the same document. In such cases, notification should be submitted at least 10 days prior to the first movement and 30 days prior to the first release. Multiple *importations* also may be described in one notification. However, all importations in a single notification must be shipped *from the same origin* and *to the same destination*. Notification of importation cannot be combined with notification of interstate movement or release.

Information to Include in a Notification

"The notification shall include the following:
(i) Name, title, address, telephone number, and signature of the responsible person;
(ii) Information necessary to identify the regulated article(s), including:
(A) The scientific, common, or trade names, and phenotype of regulated article,
(B) The designations for the genetic loci, the encoded proteins or functions, and donor organisms for all genes from which introduced genetic material was derived, and
(C) The method by which the recipient was transformed;
(iii) The names and locations of the origination and destination facilities for movement or the field site location for the environmental release; and the size of the introduction,
(iv) The date and, in the case of environmental release, the expected duration of the introduction (release); and
(v) A statement that certifies that introduction of the regulated article will be in accordance with the provisions of this section." (§ 340.3(d)(2)).

Certain information must be present in a notification to help APHIS staff determine if the proposed introduction meets eligibility criteria and performance standards. To facilitate APHIS review of this information, follow the guidelines below for organizing your information.

1. Applicant. The "applicant" is the person responsible for the information provided in the notification, who has control and will maintain control over the introduction of the regulated article to assure that Federal Regulations are met, and who certifies the notification (see **9. Certification** below). The responsible person may be a company or institution, although an individual representing the company/institution must provide their name and sign the notification.

The responsible party must be a resident of the United States, or must designate an agent who is a resident of the United States. APHIS discourages the designation of temporary employees (e.g. post-doctorates or graduate students) as responsible parties.

Applicants must provide name, title, full address, and telephone number of the primary person responsible for the introduction of the regulated article. E-mail address and fax number are

optional, but may facilitate communication. An e-mail address is required when the *ePermits* notification method is used.

2. Introduction Type. Identify whether the introduction is an importation, interstate movement, environmental release, or a combination of interstate movement and environmental release.

3. Applicant Reference Number. An applicant-supplied reference number. The purpose of this reference number is to facilitate communication regarding the status of a notification.

4. Confidential Business Information (CBI) Verification. Identify whether the submission contains CBI. If so, a CBI justification statement must be included. For more information about submission of documents containing CBI, see guidance document on **Document Submission Guidelines**. Please note that the *ePermits* system uses square brackets '[ ]' to identify CBI content. If you are submitting a notification using *ePermits*, **do not** use square brackets in your submission unless it denotes CBI content.

5. Regulated Article. Provide the common name, scientific name, and cultivar name(s) for the recipient plant. All transformed lines in a single notification must be of the same plant species. Multiple cultivars may be submitted under the same notification.

6. Phenotypic Designation. The information in this section identifies phenotype and genotype of the regulated article or articles to be introduced. Where appropriate, information should be supplied *for each group of lines having the same inserted construct.*

Phenotypic designation name. A unique identifier given to a transformed line or lines that all contain the same construct. The designation can be a name, number, short phrase, or any other unique identifier provided by the applicant to assist both the applicant and APHIS in tracking the transformed line. The designation does not have to contain information that might reveal parentage or valued characteristics. The phenotypic designation should be consistently used to identify the transformed line in all future documents submitted to APHIS, e.g. planting reports, other notifications, petitions to grant non-regulated status, etc.

Identifying lines. List all of the variety designations or identifiers for those lines to be introduced which carry a given construct.

Construct. An identifier of the genetic construct transformed into all of the lines identified above.

Mode(s) of transformation. The method used to insert the construct into the plant genome (e.g., biolistic transformation, disarmed *Agrobacterium*-mediated transformation).

Phenotype category(-ies). Please select one or more of the appropriate two-letter codes.

VR = Virus resistant
HT = Herbicide tolerant

IR = Insect resistant
FR = Fungus resistant
BR = Bacteria resistant
NR = Nematode resistant
PQ = Product quality
AP = Agronomic properties
MG = Marker genes
OO = Other

"Product quality" includes modifications such as delayed ripening of fruit, altered amino acid profile, modified seed storage proteins, enhanced floral characteristics (ornamentals), and increased solids in fruit.

"Agronomic properties" includes modifications such as drought tolerance, cold tolerance, tolerance to specific environmental stresses, enhanced nitrogen use, and male sterility.

"Other" is for modifications that do not clearly fall into one of the other categories, and has included such modifications as control lines transformed with empty vectors, alterations of gene expression for research purposes, etc.

Phenotype(s). The specific trait created by the genetic modification, and is a subset of "*phenotype category*." For example, if the category is HT, then the phenotype is resistance to a specific herbicide. If the category is VR, then the phenotype is resistance to a specific viral strain.

Genotype(s) and brief summary of construct elements. The summary of the genetic components inserted into the genome of the recipient organism, including the construct name(s) and list of construct elements. Do not abbreviate names of genetic components. For each element in a construct, in the order in which they occur in the construct, provide the following information: i) element type (e.g. promoter, gene, terminator), ii) name or function of the element (e.g. 35S promoter, extensin, catalase), iii) brief description of the element's function, iv) the organism from which the element is derived (species or virus strain). It may be convenient to present this information in a table. A single notification may include multiple constructs.

7. Introduction. This section includes details specific to each type of introduction: importation, interstate movement, and/or environmental release. Notification of interstate movements may be combined with notification of environmental release (include both sections separately), but notification of importation must be provided in a separate document.

Where the 'type of plant material' introduced is required, be as specific as possible (e.g. seeds, tubers, tissue cultures, whole plants, leaves, slips, cutting, seed potatoes, etc.).

All locations must list both county and state to facilitate information sharing with state regulatory officials and compliance with the Endangered Species Act.

Importation. Notifications of importation should have one point of origin and one destination:

POINT OF ORIGIN: Location name and complete address, including country of origin, from which the regulated article will be imported.
DESTINATION: Location name and complete address, including county and state, into which the regulated article will be imported.
DATES: The proposed dates of shipment from point of origin to destination.
QUANTITY: Type of plant material to be imported and an estimate of maximum quantity (e.g. tubers, 15 lbs.).
CONTACT PERSON(S) (optional): Name, phone number, and other contact information of a responsible person at the point of origin, destination, or both.

Interstate Movement. Notification of interstate movements may have multiple origins and destinations:

ORIGIN(S): Location name and complete address, including county and state, from which the regulated article will be moved.
DESTINATION(S): Location name and complete address, including county and state, to which the regulated article will be moved.
DATES: The proposed dates of shipment from origin to destination.
QUANTITY: Type of plant material to be moved and an estimate of maximum quantity *per movement* (e.g. tubers, 15 lbs.).
CONTACT PERSON(S) (optional): Name, phone number, and other contact information of a responsible person at any or all origins or destinations.

Environmental Release. Notification of environmental release may have multiple locations:

RELEASE LOCATION: Location name and complete address, including county and state, of the planting site. The location name must uniquely identify and distinguish the location from all other field sites to facilitate inspection. If there are multiple sites at a given address (e.g. at a farm or research plantation), the location name must be specific to the individual planting site.
GPS COORDINATES: Provide GPS coordinates for the proposed release site. Ideally this coordinate should be located close to the center of the proposed release location. If the exact location of the release site has yet to be determined, provide GPS coordinates for the boundaries that encompass the possible area that will contain the proposed release site and the area to be monitored.
RELEASE SITE HISTORY: Specify the type of agricultural activity (e.g. cropping, pasture, orchard, managed forest) and approximate length of time that the release site and area to be monitored has been under managed agricultural production.[1]
PROXIMITY TO CRITICAL HABITAT: Identify whether the proposed release site and/or area to be monitored are within designated critical habitat for a listed

[1] This information is necessary to facilitate assessment of the proposed release's possible impacts on threatened and endangered species. For additional guidance on assessment of these impacts, see *Guidance for Critical Habitat Analysis*, available online at http://www.aphis.usda.gov/brs/pdf/BRS_critical_hab_guide_notif.pdf

threatened or endangered species or within habitat proposed for designation under the Endangered Species Act (16 U.S.C., Section 1531, Endangered Species Act of 1973, as amended). If so, provide 1) the species and common names for all species that have designated critical habitat or habitat proposed for designation within the release site and monitoring area, and 2) an analysis of the effects of the proposed release on designated critical habitat or habitat proposed for designation. Indicate if the proposed release will have *no effect* or *may affect* the designated critical habitat and/or habitat proposed for designation.[1]

DURATION: The proposed dates of release/planting and final harvest/destruction of the crop. The latter date does not include any post-harvest monitoring period. Duration may be no longer than one year from the date of introduction.

SIZE OF RELEASE: Proposed total size of the release at a given site, either in area (e.g. acres, square meters, etc.) or number of propagules released (e.g. trees planted). Give both total area and area planted with transgenic crops. Area should also include any sexually compatible border rows of non-transgenic crops, if planted.

NUMBER OF PLANTINGS: If there will be multiple plantings at a given site during the proposed release period, list the number of plantings.

CONTACT PERSON(S) (optional): Name, phone number, and other contact information of a responsible person at one or more release locations.

8. Additional Information. Use this section to include any additional information that may support the applicants' certification that the regulated article will be introduced in accordance with the eligibility criteria and the performance standards set forth in 7 CFR 340.3

9. Certification. The notification must contain a signed certification that the regulated article will be introduced in accordance with the eligibility criteria and the performance standards set forth in 7 CFR 340.3. The certification must be signed and dated by the responsible party whose contact information appears in **1. Applicant** above. The certification must not stand alone on a page. A portion of at least the previous section must appear with it such that the certification can be identified as belonging to a particular notification.

An acceptable example of the certification statement is as follows:

> *I certify that the regulated article(s) described in this document will be introduced in accordance with the eligibility criteria and performance standards set forth in 7 CFR 340.3. Information contained in this document is true to the best of my knowledge. If there are any changes, I will contact APHIS promptly.*
>
> Signature _____ Date _____
> Printed Name _____

Design Protocols

Design protocols are supplemental materials that allow the applicant to describe the specific cultivation and management practices to be used in the proposed environmental release in order to meet each of the required performance standards (see **Performance Standards**). For many

crops, typical cultivation practices may not be sufficient to meet the performance standards. However, by detailing in design protocols how the applicant will alter cultivation and management practices, the applicant may be able to demonstrate that the performance standards can be met for the proposed introduction. Design protocols are not typically developed for interstate movement or importation.

APHIS may be less likely to acknowledge a notification—and thus require a permit—if, based on experience, APHIS believes that the cultivation practices typically employed for the crop would not meet the performance standards. Unlike the conditions associated with permits, design protocols are *not* enforceable conditions attached to an acknowledged notification. However, the applicant *is* responsible for meeting the performance standards described in 7 C.F.R. 340(c); failure to follow proposed design protocols may suggest that the applicant is also not meeting performance standards.

After acknowledgement, applicants *are* required to provide inspectors with on-site documentation that an introduction is meeting performance standards (see **Inspections**). Applicants are encouraged to have design protocols or similar documentation available for inspectors to help demonstrate that the introduction meets federal regulations.

Design protocols provide brief details about how the applicant intends to meet each of the six performance standards (see **Performance Standards**). Use the following as guidance for information to include in design protocols:

Performance Standard 1. Briefly describe how movements of the regulated material will be conducted to prevent dissemination during transit, and how the regulated material will be stored at the destination facility to prevent release. Include, for example, a description of packaging materials, how the materials will be identified or labeled in transit and in storage, storage location and description of the destination facilities, methods of segregation, etc. If the materials will be moved from storage to the field for release, describe how the material will be moved to prevent release in transit.

Performance Standard 2. If the article is to be released into the environment, briefly describe how the regulated material will be planted in order to prevent inadvertent mixing with other non-regulated materials. Include, for example, descriptions of how the release location is separated from adjacent plots to prevent mechanical mixing, and how planting, harvesting and other equipment will be segregated or cleaned. If seed or fruit will be produced, describe how the regulated material will be prevented from entering the food or feed supply.

Performance Standard 3. Briefly describe how the identity of the regulated materials will be maintained at all times. Include, for example, descriptions of labeling and packaging of the regulated materials, and how the release site will be identified and separated from other planting areas, using flags, stakes, markers, fallow zones, etc. Additionally, describe methods to be used to destroy or devitalize the regulated material after use (e.g. autoclaving, composting, chemical treatment), or how the regulated material will be returned to and maintained in a contained facility.

Performance Standard 4. Briefly describe how the applicant can assure that no viable vector agent is associated with the regulated material (e.g. antibiotic or other chemical treatment of tissues/cells during transformation/regeneration or of seeds, no vector agents were used).

Performance Standard 5. If the article is to be released into the environment, briefly describe the methods used to ensure that the regulated materials and any possible offspring remain confined to the designated plot and do not persist in the environment. Include, for example, descriptions of isolation distances, use of border rows or fallow zones, use of temporal isolation, cages, flower removal or bagging, male sterility, etc. In addition, describe any special circumstances that may increase the likelihood that regulated materials or offspring could persist in the environment, such as: proximity to sexually compatible wild or weedy relatives; whether the location is prone to flooding, high winds, animal incursion, or public access; if the size of the field trial is large.

Performance Standard 6. If the article is to be released into the environment, briefly describe how the field test will be terminated to reduce the likelihood of volunteers in subsequent seasons (e.g. disking, chemical treatment); and how volunteers will be managed to prevent persistence in subsequent seasons (e.g. frequency, timing, and area of monitoring, methods of removal, other crops to be planted in the field in subsequent seasons that can be readily differentiated from the regulated material).

Confidential Business Information in Notifications

General instructions for inclusion of confidential business information (CBI) in submissions to BRS are presented in the guidance document, **Document Submission Guidelines.** If a notification contains CBI, two versions of the document should be submitted to BRS: one containing CBI and another CBI-deleted version. All CBI claims must be justified in an attached justification letter. See the CBI section of the guidance document mentioned above for details on creating CBI-deleted documents and justification letters.

When sending a notification using the *ePermits* system, only the CBI version is necessary; the *ePermit* system generates the CBI-deleted version automatically. Please note that the *ePermits* system uses square brackets '[ ]' to identify CBI content. **Do not** use square brackets in your submission unless it denotes CBI content.

Only the CBI-deleted version is shared with State regulatory officials (see **APHIS Review and Acknowledgement** below). For this reason, applicants are strongly encouraged not to claim 'county' as CBI in notifications, because State regulatory officials may question the location of the introduction. In this event, the applicant may have to contact State officials directly, without APHIS' assistance, to resolve the issue. Further, any CBI claims may require FOIA office review prior to submission of the notification to the State officials.

How to Submit a Notification

If you are unable to submit notification using the *ePermits* system, notification should be mailed to:

Permit Staff
Biotechnology Regulatory Services
USDA-APHIS, Unit 91
4700 River Road
Riverdale, MD 20737

Because the certification statement on a notification must have an original signature, faxes and e-mail notifications are not accepted. In the *ePermits* system, an electronic version of a signature is collected. To facilitate processing of postal mail notifications, we also request the applicant submit an electronic file version (pdf, Word, or Word Perfect) of the non-CBI or CBI-deleted version.

Changes to a Notification after Submission

All notifications must be submitted in a complete and accurate manner. After APHIS has received a notification, changes to the notification are not accepted. An applicant may, however, *withdraw* a notification prior to acknowledgement.

In the event that the responsible person or contact information has changed or is found to be incorrect, promptly submit the revised information to APHIS in writing:

Compliance and Inspection Branch
Biotechnology Regulatory Services
USDA-APHIS, Unit 91
4700 River Road
Riverdale, MD 20737
(301) 734-0670
brscompliance@aphis.usda.gov

The letter requesting this change should include the Notification number and must bear the signature of the original responsible person, or new responsible person if changed. State regulatory officials will be notified of the change. All other changes to a notification require submission of a new notification.

If additional incorrect information is identified in an acknowledged notification, notify APHIS immediately:

Compliance and Inspection Branch
Biotechnology Regulatory Services
USDA-APHIS, Unit 91

4700 River Road
Riverdale, MD 20737
(301) 734-0670
brscompliance@aphis.usda.gov

If, after submitting a notification to APHIS the applicant decides *not* to introduce the regulated article, we request that the applicant send a letter to APHIS stating that the regulated article was not planted, as soon as possible (see also **Field Test Reports** below). This allows APHIS to document that there was no introduction and to cancel any scheduled inspections.

What to Expect After Notifying APHIS

APHIS Review and Acknowledgement

Shortly after APHIS receives a notification, APHIS assigns a case number to the submission and a biotechnologist reviews it to determine if it meets eligibility criteria and performance standards.

> "APHIS will provide copies of all notifications to appropriate State regulatory official(s) for review within 5 business days of receipt. Comments to APHIS from appropriate State regulatory officials in response to notifications for interstate movement of regulated articles will not be required by APHIS prior to acknowledgment, although States may provide their reviews to APHIS at their discretion." (**§** 340.3(e)(1)).

APHIS sends a copy of the notification to the appropriate State regulatory officials for review and comment. Although State concurrence is not required, as a courtesy APHIS does accept feedback from State regulators and considers their input before acknowledgement of a notification.

Because APHIS does not have a formal CBI-sharing arrangement with State governments, APHIS can only send the CBI-deleted copy of the notification to State regulatory officials. If State officials request access to CBI contained in a notification, APHIS encourages them to contact the applicant directly to request disclosure of the CBI.

> "(2) The Administrator, will provide acknowledgement within 10 days of receipt that the interstate movement is appropriate under notification.
> (3) The Administrator, will provide acknowledgement within 30 days of receipt that the importation is appropriate under notification.
> (4) APHIS will provide acknowledgment within 30 days of receipt that the environmental release is appropriate under notification. Such acknowledgment will apply to field testing for 1 year from the date of introduction, and may be renewed annually by submission of an additional notification to APHIS." (**§** 340.3(e)(2-4)).

After review of the notification, if APHIS agrees that the proposed introduction meets required eligibility criteria and performance standards, APHIS will issue a letter to the applicant acknowledging the appropriateness of the introduction under the notification process. APHIS will send acknowledgement letters for notification of proposed importations and environmental releases within 30 days of receipt of the notification. Acknowledgement letters for notification of interstate movement will be sent within 10 days of receipt of the notification.

The applicant must receive an acknowledgement letter that has been issued by APHIS before introducing the regulated article.

> "A person denied permission for introduction of a regulated article under notification may apply for a permit for introduction of that regulated article without prejudice." (**§** 340.3(e)(5)).

If APHIS determines that the proposed introduction is *not* appropriate for the notification process, the applicant may submit an application for an introduction *permit* without prejudice.

If an applicant has any question about whether a proposed introduction is appropriate for notification, the applicant is encouraged to contact APHIS as far in advance of the proposed introduction as possible. Although the introduction may still be eligible for a permit, approval of a permit takes more time. **Do not wait** until 30 days before your desired planting date to notify APHIS of your introduction. If your proposed introduction is determined to be inappropriate for notification and a permit is required, approval of a permit could take an additional 120 days.

Effective Dates of Acknowledged Notification

By default, an acknowledged notification is valid for one year from the date of acknowledgement. The introduction cannot proceed until on or after the date of acknowledgement, and all activities associated with the introduction (*excluding* any monitoring periods) must be completed by the expiration date. For interstate movements and importations, all shipments must have arrived at their destination before the expiration date. Environmental releases must be completely terminated by the expiration date (i.e. plants harvested, and all remaining plants and plant parts are either destroyed or moved into contained facilities).

In some cases, the applicant may wish to request that an acknowledged notification becomes effective on a specified date, such as the first proposed date of introduction. This encourages applicants to send notification to APHIS earlier, without penalizing applicants with earlier effective dates and expiration dates. Applicants should clearly state in their notification that a specific effective date is desired. In most cases this request will be granted, as long as APHIS has adequate time to acknowledge by that date. Applicants may *not* request effective dates that are sooner than the required 10- or 30-day notice periods. If an effective date is not specified, the effective date is the date of acknowledgement.

Notification of Unusual Occurrences

"The Administrator, shall be notified of any unusual occurrence within the time periods and in the manner specified in Sec. 340.4(f)(10)." (§ 340.3(d)(5)).
"APHIS shall be notified within the time periods and manner specified below, in the event of the following occurrences: (i) Orally notified immediately upon discovery and notify in writing within 24 hours in the event of any accidental or unauthorized release of the regulated article; (ii) In writing as soon as possible but not later than within 5 working days if the regulated article or associated host organism is found to have characteristics substantially different from those listed in the application for a permit or suffers any unusual occurrence (excessive mortality or morbidity, or unanticipated effect on non-target organisms)." (§ 340.4(f)(10)).

After the applicant receives APHIS acknowledgement of notification and the regulated article has been introduced, the applicant is required to notify APHIS of any unusual occurrences associated with the introduction. This is the same requirement as for introductions under permit.

In the event of any accidental or unauthorized release of the regulated article, the applicant must orally notify APHIS *immediately*, and in writing within 24 hours. Events that require immediate notification include, but are not limited to: potential dispersal of plant material outside the approved area of introduction by high winds or flooding; accidental planting of the regulated article in the wrong location; planting a variety with an unauthorized construct; damaged packaging materials; materials lost in shipping.

If the plants are observed to have any characteristics that are different from those described in the notification—particularly those characters related to plant pest risk—the applicant must notify APHIS in writing within 5 working days. Any unexpected changes in the plant's phenotype that could compromise the introduction's ability to meet eligibility criteria or performance standards should be reported. Additionally, any unexplained effects on plant heath such as crop failure or significant plant death, or unexpected impacts on non-target organisms, should be reported.

If a field trial is damaged or destroyed to the extent that the release is prematurely terminated, APHIS recommends that the written report of the unusual occurrence be combined with the required field test report (see **Field Test Report** below). Indicate clearly that the report is both a notification of the event and the final field test report.

In the event of any of these unusual occurrences, contact (orally or in writing, as required):

Compliance and Inspection Branch
Biotechnology Regulatory Services
USDA-APHIS, Unit 91
4700 River Road
Riverdale, MD 20737
(301) 734-0670
brscompliance@aphis.usda.gov

Failure to notify APHIS of unusual occurrences in the required time frames can result in legal action, civil penalties, and even criminal charges.

Inspections

> "Access shall be allowed for APHIS and State regulatory officials to inspect facilities and/or the field test site and any records necessary to evaluate compliance with the provisions of paragraphs (b) and (c) of this section." (**§** 340.3(d)(6)).

All introductions under the notification process are subject to inspection by trained federal and state inspectors. Access to field sites and related facilities (i.e. buildings for equipment, seed storage, processing, disposal, etc.) must be provided when requested by authorized personnel. Authorized inspectors may include personnel from APHIS' Biotechnology Regulatory Services or Plant Protection and Quarantine (PPQ), State Plant Health Directors, and other state personnel trained by APHIS.

Notifications are selected for inspection based upon a combination of risk-related factors, including: type of regulated article; size of the introduction (volume shipped or acreage); number of sites; experience and compliance history of the applicant; number of consecutive years of introduction under notification. Also, APHIS may conduct an inspection at any site and/or facility under notification regardless of the risk-related factors.

In addition to allowing access to facilities and field sites associated with the introduction, the responsible party is required to provide records that demonstrate that performance starndards are being met. Note that this normally requires documentation beyond the information submitted to APHIS in the notification. Applicants are encouraged to keep written field trial protocols to ensure that the introduction meets federal requirements, and documentation that these protocols are being followed (see also **Design Protocols** above).

For more information on inspections of introductions under notification, please contact:

Compliance and Inspection Branch
Biotechnology Regulatory Services
USDA-APHIS, Unit 91
4700 River Road
Riverdale, MD 20737
(301) 734-0670
brscompliance@aphis.usda.gov

28-Day Planting Report

In addition to the required field test report (below), APHIS requests that responsible parties submit a **Planting Report** within 28 days after the date of an environmental release described in an acknowledged notification. This report provides APHIS with additional detail about the *actual* releases that have taken place under an acknowledged notification. The report should include:

- Notification number
- Name of the regulated article
- Trial site (provide state, county, central GPS coordinate or address, and site identification number (if available))
- Acreage planted
- Planting date

Additionally, the report should list any sites included in the original notification that will no longer be planted. If there will be multiple planting dates, submit reports *monthly* after the first 28-day report to inform APHIS of any new plantings. Planting reports can combine information from multiple notifications; i.e. only a single report need be submitted that lists all the plantings for the previous 28 days. Reports need not be submitted when no planting occurs.

The planting report should be submitted by mail or fax to:

Compliance and Inspection Branch
Biotechnology Regulatory Services
USDA-APHIS, Unit 91
4700 River Road
Riverdale, MD 20737
Fax: (301) 734-8669

Field Test Report

"Field test reports must be submitted to APHIS within 6 months after termination of the field test. Field test reports shall include the APHIS reference number, methods of observation, resulting data, and analysis regarding all deleterious effects on plants, nontarget organisms, or the environment." (§ 7 C.F.R. 340.3 (d) (4))

All environmental releases of regulated articles under notification require the submission of a field test report within six months of the termination of the field test. Because APHIS does not always know the actual termination date in advance, APHIS considers the field test report to be due **no later than six months after the expiration of the notification**. APHIS uses this report for two purposes: 1) to have a record that the introduction was carried out and terminated according to federal regulations, and 2) to collect data about any observed unanticipated impacts the field trial may have had, if any. Note that this reporting requirement only applies to environmental releases under notification (not importations or interstate movements).

The following information should be included in the field test report:

- APHIS reference number
- Listing of lines planted
- The location in which the observations were made
- A brief description of the types of observations that were made:
    - What characters were observed?

  - How where they rated?
  - How frequently was the field monitored?
- A summary of the data that was gathered during the field season.
- A summary of the analysis of the collected data.
- Analysis of any deleterious effects that were observed during the field season
  - Effects on plants
  - Effects on non-target organisms
  - Effects on the environment.
- A summary of the final disposition of the regulated material.

Unusual occurrences during an introduction may require immediate notification to APHIS, particularly when related to possible accidental release or if plant characteristics are found to be different from those described in the original notification (see **Notification of Unusual Occurrences** above). The field test report, however, requires the applicant to report any additional deleterious effects observed 'on plants, nontarget organisms, or the environment,' with a description of data collection and analytical methods used to characterize those effects.

Field trials under notification lasting longer than one year from the date of introduction (i.e. for perennial crops) are permitted if the applicant submits a notification each year (see **Effective Dates of Acknowledged Notifications** above). In such cases, there is no true 'termination' of the first year's field trial. However, because subsequent years are separate notifications, the applicant should submit an 'interim' field test report within six months of the end of each notification year.

If, after a notification has been acknowledged by APHIS, the applicant decides *not* to introduce the regulated article, we request that the applicant send a letter to APHIS stating this as soon as possible. This allows APHIS to document that the introduction did not proceed and to cancel any scheduled inspections. APHIS accepts this letter in lieu of the required field test report in the case of introductions that are acknowledged but that did not take place.

If *all* lines in an ongoing field trial under notification are granted non-regulated status, the applicant must submit a field test report covering the period from introduction to the date that non-regulated status is granted. In addition to the information required by 7 CFR 340.3(d)(4), the report should state that the environmental release has been administratively terminated due to the granting of non-regulated status (include petition number). The environmental release may still be subject to inspection until the final field test report has been received. Further, if the environmental release contains any additional lines that have *not* been granted non-regulated status, the environmental release is still subject to all regulations in 7 CFR 340.3.

The field test report should be submitted by mail or fax to:

Compliance and Inspection Branch
Biotechnology Regulatory Services
USDA-APHIS, Unit 91
4700 River Road
Riverdale, MD 20737

Fax: (301) 734-8669

How to Find More Information

If you would like more information about introductions using the notification procedure, please contact:

Environmental Risk Analysis Programs
Biotechnology Regulatory Services
USDA-APHIS, Unit 147
4700 River Road
Riverdale, MD 20737
Neil.E.Hoffman@aphis.usda.gov
(301) 734-6331

For information about a specific notification you have already submitted to APHIS-BRS, please contact:

Permit Staff
Biotechnology Regulatory Services
USDA-APHIS, Unit 91
4700 River Road
Riverdale, MD 20737
(301) 734-4878

Notification

Additional Materials

Sample Interstate Movement Notification

Sample Import Notification

Sample Environmental Release Notification

The sample documents included in this section are fictional and for educational purposes. Any similarity to real persons, companies, or technologies is coincidental.

U.S. DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE
BIOTECHNOLOGY REGULATORY SERVICES

BRS NOTIFICATION - INTRODUCTION OF GENETICALLY ENGINEERED PLANTS

1. NAME, ADDRESS, TELEPHONE, AND EMAIL OF APPLICANT

Name: Dr. Pam Pinders
Position:
Organization: Earthnut LLC
Organization Unique ID:
Address: Route 7
Nuttall Hiils, GA 12345
County/Province:
Township/Island:

Day Telephone: 404-555-1212
FAX:
Alternate:

Email 1: Pam@earthnut.com
Email 2:

2. INTRODUCTION TYPE

- [ ] Importation
- [x] Interstate Movement
- [ ] Interstate Movement and Release
- [ ] Release

3. APPLICANT REFERENCE NUMBER

4. CONFIDENTIAL BUSINESS INFORMATION VERIFICATION (CBI)

Does this application contain CBI? [ ] Yes [x] No

CBI Justification:

N/A

5. REGULATED ARTICLE

Scientific Name: Arachis hypogaea
Common Name: Peanut
Cultivar and/or Breeding Line: Sweet Georgia Brown

6. PHENOTYPIC DESIGNATION

1) **Phenotypic Designation Name:** BR 549
Identifying Line(s): AHT001, AHT002, AHT003
Construct(s): pNC123
Mode of Transformation: Biolistic

Phenotype(s)

MG - Visual marker

Genotype(s)

Gene(s) of Interest

Promoter: 35S **from** Cauliflower mosaic caulimovirus - Enhanced 35S

Gene: Green fluorsecent protein **from** Aequorea victoria - GFP from Aequorea victoria (Jellyfish)

Terminator: Nopaline synthase **from** Agrobacterium tumefaciens - NOS 3' from T-DNA

7. INTRODUCTION

Point of Origin

Location Name & Description	Location Address	Contact(s)
1) Peanut Breeding Inc.	123 Groundnut Lane Chinkapin Hickory, North Carolina 54321 **County:** Chinkapin	1) Mr. Goober Peabody Peanut Breeding Inc. 123 Groundnut Lane Hickory, North Carolina 54321 **Day Telephone:** 919-555-1212 **Email 1:** Gpeabody@peanutsinc.com

Destination

Location Name & Description	Location Address	Contact(s)

1) Earthnut LLC	Route 7 Huttall Hills, Georgia 12345 **County:** Kubakim **Proposed Start Date:** 6/1/2007 **Proposed End Date:** 6/1/2008 **Quantity:** 20 Lbs Seeds	**1)** Dr. Pam Pinders Route 7 Nuttall Hills, Georgia 12345 **Day Telephone:** 404-555-1212 **Email 1:** Pam@earthnut.com

8. ADDITIONAL INFORMATION

Example of Interstate Movement Notification

I, *Pam Pinders*, certify that the regulated article will be introduced in accordance with the eligibility criteria and the performance standards set forth in 7 CFR 340.3. The above information is true to the best of our knowledge.

I acknowledge this is not an application to move or import select agents, the genes expressing select agents, or the toxins made by the select agents, as described in 9 CFR 121.

If there are any changes to the information disclosed in this application, I will contact APHIS.

9. SIGNATURE OF RESPONSIBLE PERSON	**10. DATE**

U.S. DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE
BIOTECHNOLOGY REGULATORY SERVICES

BRS NOTIFICATION - INTRODUCTION OF GENETICALLY ENGINEERED PLANTS

1. NAME, ADDRESS, TELEPHONE, AND EMAIL OF APPLICANT

Name: Dr. Joe Scientist
Position:
Organization: A Major University
Organization Unique ID:
Address: 2005 Research Drive
Bluefield, MD 12345
County/Province:
Township/Island:

Day Telephone: 301-555-1212
FAX:
Alternate:

Email 1: Joe@university.edu
Email 2:

2. INTRODUCTION TYPE

- [x] Importation
- [ ] Interstate Movement
- [ ] Interstate Movement and Release
- [ ] Release

3. APPLICANT REFERENCE NUMBER

4. CONFIDENTIAL BUSINESS INFORMATION VERIFICATION (CBI)

Does this application contain CBI? [ ] Yes [x] No

CBI Justification:

N/A

5. REGULATED ARTICLE

Scientific Name: Tagetes erecta

Common Name: Marigold

Cultivar and/or Breeding Line:

6. PHENOTYPIC DESIGNATION

1) **Phenotypic Designation Name:**

Identifying Line(s): TE 001

Construct(s): BG 456

Mode of Transformation: Biolistic

Phenotype(s)

PQ - Flower color altered

Genotype(s)

Gene(s) of Interest

Promoter: 35S **from** Cauliflower mosaic caulimovirus - Enhances 35S

Enhancer: Upstream sequence from 35S promoter **from** Cauliflower mosaic caulimovirus - Additional upstream sequence from 35s promoter

Gene: Flavoniod hydrolase **from** Viola sp. (Pansy) - Flavonoid 3' - 5' hydroxylase

Terminator: Nopaline synthase **from** Agrobacterium tumefaciens - nos 3' region from T-DNA

Selectable Marker

Promoter: Nopaline synthase **from** Agrobacterium tumefaciens - nos promoter from T-DNA

Gene: Neomycin phosphotransferase **from** Escherichia coli - NPT II

Terminator: Nopaline synthase **from** Agrobacterium tumefaciens - nos 3' region

7. INTRODUCTION

Point of Origin

Location Name & Description	Location Address	Contact(s)

1) BlueGenes Corporation LTD	123 Blue Mountain Road Leura, Australia **County:** NSW	

Destination

Location Name & Description	Location Address	Contact(s)
1) University Research	2005 Research Drive Bluefield, Maryland 12345 **County:** Azure **Proposed Start Date:** 6/1/2007 **Proposed End Date:** 6/1/2008 **Quantity:** 20 Vessels Tissue culture containers	

8. ADDITIONAL INFORMATION

Importation example

I, *Joe Scientist*, certify that the regulated article will be introduced in accordance with the eligibility criteria and the performance standards set forth in 7 CFR 340.3. The above information is true to the best of our knowledge.

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9. SIGNATURE OF RESPONSIBLE PERSON	**10. DATE**

U.S. DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE
BIOTECHNOLOGY REGULATORY SERVICES

BRS NOTIFICATION - INTRODUCTION OF GENETICALLY ENGINEERED PLANTS

1. NAME, ADDRESS, TELEPHONE, AND EMAIL OF APPLICANT

Name: Mr. Russ Solanum
Position:
Organization: Pa's Potatoes, Inc.
Organization Unique ID:
Address: 2004 Chippewa Rd.
Baker Hill, ME 12345
County/Province: Hancock
Township/Island:

Day Telephone: 301-555-1212
FAX:
Alternate:

Email 1: Russ@taters.com
Email 2:

2. INTRODUCTION TYPE

- [ ] Importation
- [ ] Interstate Movement
- [ ] Interstate Movement and Release
- [x] Release

3. APPLICANT REFERENCE NUMBER

4. CONFIDENTIAL BUSINESS INFORMATION VERIFICATION (CBI)

Does this application contain CBI? [ ] Yes [x] No

CBI Justification:

N/A

5. REGULATED ARTICLE

Scientific Name: Solanum tuberosum

Common Name: Potato

Cultivar and/or Breeding Line: Gem Russet

6. PHENOTYPIC DESIGNATION

1) **Phenotypic Designation Name:** VR67
Identifying Line(s): ST001, ST002, ST003
Construct(s): pCP123
Mode of Transformation: Agrobacterium tumefaciens, disarmed

Phenotype(s)

VR - Potato Y potyvirus resistant

Genotype(s)

Gene(s) of Interest

Promoter: 35s **from** Cauliflower mosaic caulimovirus - Enhanced 35s 5'

Gene: Potato virus Y coat protein **from** Potato Y potyvirus, Strain 0 - Coat protein from potato virus Y - Gene is in sense orientation.

Terminator: Nopaline synthase **from** Agrobacterium tumefaciens - Nos 3' from Agrobacterium T-DNA

Screenable Marker

Promoter: 35s **from** Cauliflower mosaic caulimovirus - Enhanced 35S 5'

Gene: Beta-glucuronidase **from** Escherichia coli - GUS gene from E. coli

Terminator: Nopaline synthase **from** Agrobacterium tumefaciens - Nos 3' from Agrobacterium T-DNA

2) **Phenotypic Designation Name:** Potato Y potyvirus resistant
Identifying Line(s): ST004, ST005, ST006
Construct(s): pCP456
Mode of Transformation: Agrobacterium tumefaciens, disarmed

Phenotype(s)

VR - Potato Y potyvirus resistant

Genotype(s)

Gene(s) of Interest

Promoter: 35S **from** Cauliflower mosaic caulimovirus - Enhanced 35 S 5'

Gene: Potato virus Y coat protein **from** Potato Y potyvirus, Strain 0 - Potato virus Y coat protein in antisense orientation

Enhancer: Alcohol dehydrogenase intron 1 **from** Zea mays - An intron from maize adh

Terminator: Nopaline synthase **from** Agrobacterium tumefaciens - Nos 3' from Agrobacterium T-DNA

Selectable Marker

Promoter: 35S **from** Cauliflower mosaic caulimovirus - 35S 5' from CaMV

Gene: Phosphinothricin acetyltransferase **from** Streptomyces hygroscopicus - Bar gene

Terminator: Nopaline synthase **from** Agrobacterium tumefaciens - Nos terminator

7. INTRODUCTION

Release Site

Location Name & Description	Location Address	Contact(s)
1) Russ Burbank's Farm	1776 Yukon Lane Tuber, Idaho 12345 **County:** Bingham **Proposed Field Test Start Date:** 6/1/2007 **Proposed Field Test End Date:** 6/1/2008 **Number of Proposed Plantings:** 1 **Quantity:** 50 Acres	

Provide GPS Coordinates for the proposed release site. Ideally this should be located close to the center of the proposed release location. If the exact location of the release site has yet to be determined, provide GPS coordinates for the boundaries that encompass the possible area that will contain the proposed release site and the area to be monitored.

Location GPS Coordinates: 42 53 33 N, 112 28 19 W

Approximately how long (years) has the release site and area to be monitored been under managed agricultural production? Specify the type of agricultural activity - e.g. cropping, pasture, orchard, managed forest.

Release Site History: A research farm that has been under agricultural production for more than 50 years.

Is the proposed release site and/or the area requiring monitoring (or the area within the boundaries of the possible release/monitoring area for sites where the release has yet to be determined) within designated critical habitat for a listed threatened or endangered species or within habitat proposed for designation under the Endangered Species Act (16 U.S.C., Section 1531, Endangered Species Act (ESA) of 1973, as amended)?

Answer Accordingly: ___ Yes _X_ No

If "Yes" to above question, provide the genus/species name and common name for all species that have designated critical habitat or habitat proposed for designation within the release site and monitoring area.

If "Yes" to above question, provide an analysis of the effects of the proposed release on designated critical habitat and habitat proposed for designation. Indicate if the proposed release will have "no effect on" or "may affect" the designated critical habitat and/or habitat proposed for designation.

8. ADDITIONAL INFORMATION

Example of a release Notification

I, *Russ Solanum*, certify that the regulated article will be introduced in accordance with the eligibility criteria and the performance standards set forth in 7 CFR 340.3. The above information is true to the best of our knowledge.

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If there are any changes to the information disclosed in this application, I will contact APHIS.

9. SIGNATURE OF RESPONSIBLE PERSON	**10. DATE**

Notification

Version History

1/16/2007	Original draft.
9/7/2007	Reformatting to match ePermits (p. 16-20). Addition of guidance on TES data requirements (p. 19). Addition of guidance on design protocols (p. 21-22). Addition of sample notifications.
11/20/2007	Reformatting to remove references to chapter organization of *BRS User's Guide*
2/5/2008	Removal of word "draft" from document