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

Guidance for APHIS Permits for Field Testing or Movement of Organisms Intended for Pharmaceutical or Industrial Use

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I. PHARMACEUTICAL & INDUSTRIAL PERMIT PROCESS OVERVIEW

A. Overview of Applicant activities and APHIS oversight of the environmental release of regulated articles

Applicant	APHIS
• Optional early consultation with APHIS • Familiarize with pertinent regulations and APHIS guidance documents • Gather information requested in permit application • Determine environmental release site location • Design confinement conditions for environmental release • Write Standard Operating Procedures (SOPs) • Identify employees and training required for those employees • Submit Permit at least 120 days prior to release if no Environmental Assessment (EA) is required, 180 days if EA is required • Provide addition information requested by APHIS • Revise procedures, SOPs and training as requested by APHIS • Train Employees • Receive Approved Permit with attached APHIS permit and APHIS supplemental permit conditions • Complete training of employees and train any new employees during the environmental release • Keep records of training • Submit reports to APHIS during the environmental release as specified in the APHIS permit conditions and APHIS supplemental permit conditions • Conduct environmental release as described in the regulations, permit, APHIS permit conditions, APHIS supplemental permit conditions and SOPs • Keep records of actions during the environmental release as specified in the permit, permit conditions and supplemental permit conditions • Monitor and keep records of monitoring the environmental release site for volunteers	• Optional early consultation with Applicant • Discussions with applicant on procedures and processes required for proposed field test • Receive permit application and review for administrative completeness • Request further information for administrative completeness • Assign Biotechnologist for scientific review • Scientific Review of permit, SOPs and training of personnel • Request changes to the permit application or procedures as required by APHIS • Request consultations if necessary • Determine if environmental release requires Environmental Assessment (EA) or Environmental Impact Statement (EIS), before permit can be issued • If EA is required, write EA, publish EA in the Federal Register for Public Comment, respond to public comments and determine if APHIS can reach a Finding of No Significant Impact (FONSI) • Send letter to state notifying of permit application • Receive state response and work with state if issues are raised • Determine if permit can be issued and if so issues permit • Inspect field trial site at all critical control points before, during, and after release of the regulated article • Review records and observe field trial operations to assure that all permit conditions are met including, training, planting, monitoring, cleaning, reproductive control, harvest, and movement • Follow up on all noncompliance incidents and review corrective actions implemented to assure compliance with all Federal Regulations • Review reports or records of potential harmful effects on the environment • Determine that permit conditions for devitalization and disposal of the regulated article are fully met • Review reports submitted by permittee

B. Achieving compliance

Several components work in concert to meet compliance with the regulations:

- APHIS educates applicants about the requirements of the regulation to facilitate compliance
- Applicants train their employees and cooperators about required procedures to be followed using APHIS-approved training
- Applicants employ field operation processes using APHIS-approved Standard Operating Procedures (SOPs).
- Applicants monitor the site and maintain accurate records to demonstrate full achievement of all permit conditions.
- APHIS reviews applicant reports to ensure compliance and considers any changes that might be needed for future tests
- APHIS inspects throughout the field test, focusing on critical points in production, to verify that all permit conditions have been met and confinement of the regulated article has been maintained.
- APHIS follows up on all potential deviations from Federal Regulations, and observations of deleterious or harmful effects related to the introduction of the regulated article.
- Applicants submit periodic reports to APHIS providing information critical to maintaining compliance with Federal Regulations.

II. LIST OF ABBREVIATIONS

APHIS	Animal and Plant Health Inspection Service
BRS	Biotechnology Regulatory Services
CBI	Confidential Business Information
CDC	Centers for Disease Control and Prevention
CFR	Code of Federal Regulations
EA	Environmental Assessment
EPA	Environmental Protection Agency
FDA	Food and Drug Administration
FONSI	Finding of No Significant Impact
HHS	United States Department of Health and Human Services
NIH	National Institutes of Health
PPA	Plant Protection Act
PPQ	Plant Protection and Quarantine
SOP	Standard Operating Procedures
SPRO	State Plant Regulatory Official
TES	Threatened and Endangered Species
USDA	United States Department of Agriculture
USC	United States Code

III.INTRODUCTION

A. Purpose and Scope

This guidance document prepared by the Animal and Plant Protection Service (APHIS) within the U.S. Department of Agriculture (USDA) is intended to provide guidance for field testing and movement of organisms engineered to produce compounds intended for industrial or pharmaceutical use. Biotechnology Regulatory Services (BRS) within APHIS regulates the importation and interstate movement, and the release into the environment (outside of a contained facility, such as a greenhouse, growth chamber, laboratory or fermentor) of regulated genetically engineered organisms. APHIS requires the submission and approval of a Form 2000 permit application prior to introduction of these regulated articles. The information and data submitted by the applicant in Form 2000 describe in detail the processes and procedures that will be used to confine the regulated article to the field test site and to contain the regulated article when it is moved. APHIS reviews the information submitted in the Form 2000 by the permit applicant; and APHIS may request additional procedures or information. Following review, APHIS may determine that an environmental assessment (EA) or environmental impact statement (EIS) is required prior to issuance of a permit. If a Form 2000 permit application is approved by APHIS, the field test or movement may proceed in accordance with the procedures put forth in the permit and the APHIS permit and supplemental conditions, to prevent escape, dissemination and persistence of the regulated article into the environment.

APHIS requirements to conduct field tests or move organisms engineered to produce compounds intended for industrial or pharmaceutical use were strengthened and published for public comment in March 2003. These changes increased the stringency of conditions required to handle these regulated materials. Accordingly, the amount of data required for submission of a Form 2000 permit application and the procedures used for field testing and movement of these organisms has increased in the last few years. This guidance document provides information that an applicant should consider for addressing containment (to a facility such as a laboratory or greenhouse or during movement), confinement (to the field test site), and environmental issues.

To aid APHIS Form 2000 permit applicants in the past, BRS published on its website a number of letters that updated information requirements and mitigation measures required for field testing genetically engineered organisms intended for an industrial or pharmaceutical purpose. This guidance document consolidates and updates the previously published guidance letters and serves as a vehicle for BRS to convey future changes in its regulatory policy regarding these regulated articles. When this guidance is so updated, a notice will be published on the BRS website summarizing the changes made. In addition to providing assistance to applicants, this guidance document will serve to provide transparency in BRS' processes and thereby help to address the current level of public interest in the regulatory oversight of genetically engineered organisms. Additional guidance on the regulation of plants expressing pharmaceuticals or biologics by APHIS and the Food and Drug Administration (FDA) can be found in the FDA/USDA Draft Guidance for Industry: Drugs, Biologics, and Medical Devices derived from Bioengineered Plants for Use in Humans and Animals at http://www.fda.gov/cber/gdlns/bioplant.pdf.

B. Regulatory Summary

The regulations in Code of Federal Regulations (7 CFR 340) (http://www.access.gpo.gov/nara/cfr/waisidx_08/7cfr340_08.html) under the Plant Protection Act (PPA) (7 U.S.C. 7701-7772) govern the introduction of regulated articles.

Note: text boxes in this document highlight text from Federal Register Notices and the Federal Code of Regulations.

Introduce or Introduction is defined as:

To move into or through the United States, to release into the environment, to move interstate, or any attempt thereat. 7 CFR 340.1

A regulated article is defined as:

Any organism which has been altered or produced through genetic engineering, if the donor organism, recipient organism, or vector or vector agent belongs to any genera or taxa designated in 340.2 and meets the definition of plant pest, or is an unclassified organism and/or an organism whose classification is unknown, or any product which contains such an organism, or any other organism or product altered or produced through genetic engineering which the Administrator, determines is a plant pest or has reason to believe is a plant pest. Excluded are recipient microorganisms which are not plant pests and which have resulted from the addition of genetic material from a donor organism where the material is well characterized and contains only non-coding regulatory regions. 7 CFR 340.1

The introduction of a regulated article producing compounds intended for pharmaceutical or industrial use is prohibited unless authorized by an APHIS Form 2000 Permit. Beginning with the 2003 growing season, growing and handling processes were modified for the introduction of regulated articles producing pharmaceutical and industrial compounds (March 10, 2003 Federal Register Notice, 68 FR 11337-11340 available at http://www.aphis.usda.gov/brs/pdf/7cfr.pdf Accordingly, APHIS regulatory requirements were strengthened with regard to permit confinement measures, procedures to verify compliance, and ways to enhance the transparency of the permitting system.

C. Definition of Pharmaceutical Intent

To clarify the meaning of pharmaceutical intent, APHIS has provided the following working definition: If commercialization of the product will require approval from FDA's Center for Biologics Evaluation and Research (for human biologics), Center for Drug Evaluation and Research (for human drugs), Center for Veterinary Medicine (for animal drugs), or USDA's Center for Veterinary Biologics (for animal biologics), then the organism is considered to have been engineered with pharmaceutical intent.

D. Definition of Industrial Compounds

For purposes of this rule, plants engineered to produce industrial compounds include those plants that meet the following three criteria: (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. 68 FR 46434- 46436. http://www.aphis.usda.gov/brs/fedregister/BRS_20030806a.pdf

Genetically engineered plants designed to produce industrial compounds should be introduced under Form 2000 Permit and no longer qualify under notification (http://www.aphis.usda.gov/brs/fedregister/BRS_20050504a.pdf). Industrial uses include, but are not limited to, detergent manufacturing, paper production, and mineral recovery.

E. Mineral Recovery

Applicants are encouraged to consult with BRS for traits involving mineral recovery to determine if these require a Form 2000 Permit or are covered under the notification process. The term mineral recovery has been interpreted by BRS in terms of the intended use of the engineered plant. For instance plants would require Form 2000 Permits, when engineered for phytoremediation where the plants are not intended for final use in food or feed. In other cases when crops are intended for food or feed use that are engineered for tolerance to high metals or stress, these may qualify for notification.

F. Scope of the Form 2000 Permit

The Form 2000 Permit does not eliminate the applicant's legal responsibility to obtain all necessary Federal and State approvals, including for: (A) the use of any non-genetically engineered plant pest or pathogens as challenge inoculum; (B) plants, plant parts or seeds which are under existing Federal or State quarantine or restricted use; (C) experimental use of unregistered chemicals; and (D) food, feed, pharmacological, biologic, or industrial use of regulated articles or their products and co-mingled plant material. For further information for (A) and (B) consult APHIS PPQ http://www.aphis.usda.gov/ppq/permits/plantpest/pathogen.html. For further information for (C) and (D) depending on the use, reviews by APHIS, the FDA, or the EPA may be necessary.

G. Pests and Pathogens or DNA from Pests and Pathogens That May Be Select Agents

Under the Agricultural Bioterrorism Protection Act, entities that possess, use, or transfer agents or toxins deemed a severe threat to animal or plant health or products must notify and register with USDA. APHIS has been designated as the agency responsible for implementing the provisions of the law for USDA. Under the Public Health Security and Bioterrorism Preparedness Response Act, entities that possess, use, or transfer toxins or agents deemed a threat to public health must register with HHS. The Centers for Disease Control and Prevention (CDC)s has been designated by the United States Department of Health and Human Services (HHS) as the agency responsible for implementing the provisions of the law for HHS. To determine if the donor organism (the organism from which genetic material is obtained for transfer to the recipient organism) or recipient organism or product poses a severe threat to public health, animal or plant health, refer to the APHIS website (http://www.aphis.usda.gov/programs/ag_selectagent/index.html). For organisms or products that are designated a select agent, applicants are advised to contact the relevant persons indicated on the APHIS website for further information before submitting an application. Applications to move or import select agents, the genes expressing select agents, or the toxins made by the select agents are not eligible for a notification and must be applied for under permit.

IV. ADMINISTRATIVE ACTIONS ON A FORM 2000 PERMIT

A. Time Frame for Review, Issuance and Duration of the Permit

Permit for release into the environment. An application for the release into the environment of a regulated article shall be submitted at least 120 days in advance of the proposed release into the environment. An initial review shall be completed by APHIS within 30 days of the receipt of the application. If the application is complete, the responsible individual shall be notified of the date of receipt of the application for purposes of advising the applicant when the 120 day review period commenced. (The 120 day review period would be extended if preparation of an environmental impact statement in addition to an environmental assessment was necessary.) If the application is not complete, the responsible individual will be advised what additional information must be submitted. APHIS shall commence the 120 day review period upon receipt of the additional information, assuming the additional information submitted is adequate. When it is determined that an application is complete, APHIS shall submit to the State department of agriculture of the State where the release is planned, a copy of the initial review and a copy of the application marked, "CBI Deleted", or "No CBI" for State notification and review. (Application forms are available without charge from the Animal and Plant Health Inspection Service, Plant Protection and Quarantine, Biotechnology and Scientific Services, Biotechnology Permits, 4700 River Road, Unit 147, Riverdale, Maryland 20737–1 237, or from local offices which are listed in telephone directories. A person should specify in requesting the application that the permit is for the introduction of a regulated article subject to regulation under part 340.) 7 CFR 340.4(b)

Limited permits for interstate movement or importation of a regulated article. An application for the interstate movement or importation of a regulated article shall be submitted at least 60 days in advance of the first proposed interstate movement and at least 60 days prior to each importation. An initial review shall be completed by APHIS within 15 days of the receipt of the application. If the application is complete, the responsible person shall be notified of the date of receipt of the application for purposes of advising the applicant when the 60 day review period commenced. If the application is not complete, the responsible person will be advised what additional information must be submitted. APHIS shall commence the 60 day review period upon receipt of the additional information, assuming the additional information submitted is adequate. When it is determined that an application is complete, APHIS shall submit to the State department of agriculture of the State of destination of the regulated article a copy of the initial review and the application marked, "CBI Deleted", or "No CBI" for State notification and review. 7 CFR 340.4(b)

Administrative action on applications. After receipt and review by APHIS of the application and the data submitted pursuant to paragraph (a) of this section, including any additional information requested by APHIS, a permit shall be granted or denied. If a permit is denied, the applicant shall be promptly informed of the reasons why the permit was denied and given the opportunity to appeal the denial in accordance with the provisions of paragraph (g) of this section. If a permit is granted, the permit will specify the applicable conditions for introduction

of the regulated article under this part. 7 CFR 340.4(b)

Separate Form 2000 Permit applications are required for release into the environment (release permits) or for interstate movement and importation (movement permits). An APHIS permit number will be assigned to the permit. APHIS permit numbers end in the letter "r" for release permits and "m" for movement permits. In all correspondence relating to the permit, include the permit number in the correspondence; in e-mail correspondence, include the APHIS permit number in the subject heading.

For pharmaceutical and industrial Form 2000 permits, a new permit should be submitted every year, even if the same regulated article is released in the same location year after year. In section 8 of the form, applicants should indicate the inclusive dates of the introduction. If it is desirable to have the introduction authorized at the earliest possible date, indicate “ASAP” (As Soon As Possible). In that case the permit will be authorized on the same date the administrative review is completed as has been done in the past. If it is desirable to have the introduction begin on a specific date, for example, to continue a permit submitted from a previous year, enter the desired date for the authorization to begin. In the event your application is not issued by Biotechnology Regulatory Services prior to the requested start date, then the effective start date will default to the date issued and will expire 1 year from that date.

Forward dating represents a change in APHIS/BRS processing of permits. This change may be particularly useful for movement permits to eliminate overlaps between successive permits. Also it is a means to encourage early submissions as the effective date is determined by the applicant independent of the review process. By approving permits in advance of the authorization, APHIS seeks to provide a mechanism to facilitate planning for the applicant. The effective date will be indicated in the “Date” section of “For APHIS Use Only” section on the first page of the Form 2000 Permit application. The expiration date, normally 12 months from the effective date, is indicated in the box marked expiration date.

Release permit applications should be submitted at least 120 days before the planned release date. Contact APHIS as early as possible if an EA or EIS might be needed. Refer to the section below on Environmental Assessments for information on when EAs may be required. Movement permit applications should be submitted at least 60 days before the planned movement date. Permit applications will be reviewed for completeness within 15 days for movement and within 30 days for release permit applications. In either case, if the application is complete, the responsible person (=applicant) should be notified of the date of receipt of the application for purposes of advising the applicant when the review period commenced. If the application is not complete, the responsible person will be advised as to what additional information should be submitted. When it is determined that an application is complete, APHIS will submit, to the State Plant Regulatory Official (SPRO) of the state of destination or site of release, a copy of the CBI-deleted permit. If a permit is granted, the applicant will be notified and the permit will specify the conditions of release or movement.

B. Withdrawing a Permit or Denial of a Permit

Withdrawal or denial of a permit. Any permit which has been issued may be withdrawn by an inspector or the Administrator if he/she determines that the holder thereof has not complied with

one or more of the conditions listed on the permit. APHIS will confirm the reasons for the withdrawal of the permit in writing within ten (10) days. Any person whose permit has been withdrawn or any person who has been denied a permit may appeal the decision in writing to the Administrator within ten (10) days after receiving the written notification of the withdrawal or denial. The appeal shall state all of the facts and reasons upon which the person relies to show that the permit was wrongfully withdrawn or denied. The Administrator shall grant or deny the appeal, in writing, stating the reasons for the decision as promptly as circumstances allow. If there is a conflict as to any material fact, a hearing shall be held to resolve such conflict. Rules of practice concerning such a hearing will be adopted by the Administrator. 7 CFR 340.4 (g)

A permit application may be withdrawn by the applicant at any time after the submission and prior to permit issuance. If the permit application is denied, APHIS will inform the applicant the reasons for the denial and give the applicant the opportunity to appeal the denial. In such cases the permit applicant should inform APHIS in writing of the decision to withdraw the permit.

C. Decision Not to Plant at a Field Test Site

Following issuance of the permit, if the permit applicant decides not to plant a field test that was proposed for planting in the permit, the responsible party should notify APHIS/BRS in the 28 day planting report any sites that will not be planted. If no planting will occur or the decision not to plant was not made when the 28 day planting report was submitted, notify APHIS/BRS in writing following procedures for the 28 day planting report. Responsible parties are encouraged to report to APHIS/BRS decisions not to plant in a timely manner to avoid APHIS inspections of field test sites that will not be planted.

V. FORMATTING, SUBMITTING AND AMENDING A FORM 2000 PERMIT

APHIS's regulations at 7 CFR part 340 state that a person who is issued a permit shall comply not only with the standard permit conditions in the regulations (7 CFR § 340.4 (f)), but also any supplemental conditions which are listed on the permit. Field test permits include detailed descriptions of the conditions under which the permit is issued. These conditions address movement of the regulated articles to the field test site, how the conduct the field test is conducted, and then any movement of the regulated articles to facilities where the compounds of interest are extracted. Field release permit conditions are designed to confine the regulated articles to the test site during the test and ensure that they do not persist in the environment beyond the conclusion of the field tests. On March 10, 2003 (68 FR 11337 – 1134) APHIS published for public comment permit conditions pertaining to scientific issues to achieve confinement and the ways APHIS administers the program for pharmaceutical and industrial permits. These changes are reflected in the Standard Operating Procedures (SOPs), Personnel Training Program, confinement conditions as contained in this section. When submitting a permit application to APHIS for the release into the environment of a regulated article engineered to produce compounds intended for industrial or pharmaceutical use, applicants are required to submit an APHIS Form 2000 Permit application, SOPs and Personnel Training Program.

An electronically writable portable document format (pdf) version of the APHIS Form 2000 is

available online at http://www.aphis.usda.gov/brs/pdf/2000.pdf. Submit two copies of the permit application including all required SOPs, data, and personnel training programs. Sequentially number all pages in the submission. State the review status of the product with other regulatory agencies. Cited literature does not need to be submitted unless it provides information for addressing Form 2000 permit section 1 3a-i. Cited literature may be requested by APHIS during the review process when this would expedite permit application review.

APHIS encourages the submission of a completed permit application with all data for review. However, if all the information such as the field site pending grower contract negotiation or all SOPs pending acquisition of farm equipment is not available at the time the permit application is submitted, the partial permit application may be submitted so that the review process can begin. Indicate what additional material will be submitted. Send the completed Form 2000 Permit application request to: Permit Specialist, U.S. Department of Agriculture, Animal and Plant Health Inspection Service, BRS, Unit 91, 4700 River Road, Riverdale, MD 20737-1237.

The application shall include the following information:
(1) Name, title, address, telephone number, signature of the responsible person and type of permit requested (for importation, interstate movement, or release into the environment);
(2) All scientific, common, and trade names, and all designations necessary to identify the: Donor organism(s); recipient organism(s); vector or vector agent(s); constituent of each regulated article which is a product; and, regulated article;
(3) Names, addresses, and telephone numbers of the persons who developed and/or supplied the regulated article;
(4) A description of the means of movement (e.g., mail, common carrier, baggage, or hand carried (and by whom));
(5) A description of the anticipated or actual expression of the altered genetic material in the regulated article and how that expression differs from the expression in the non-modified parental organism (e.g., morphological or structural characteristics, physiological activities and processes, number of copies of inserted genetic material and the physical state of this material inside the recipient organism (integrated or extrachromosomal), products and secretions, growth characteristics);
(6) A detailed description of the molecular biology of the system (e.g., donor-recipient-vector) which is or will be used to produce the regulated article;
(7) Country and locality where the donor organism, recipient organism, vector or vector agent, and regulated article were collected, developed, and produced;
(8) A detailed description of the purpose for the introduction of the regulated article including a detailed description of the proposed experimental and/or production design;
(9) The quantity of the regulated article to be introduced and proposed schedule and number of introductions;
(10) A detailed description of the processes, procedures, and safeguards which have been used or will be used in the country of origin and in the United States to prevent contamination, release, and dissemination in the production of the: Donor organism; recipient organism; vector or vector agent; constituent of each regulated article which is a product; and regulated article;
(11) A detailed description of the intended destination (including final and all intermediate destinations), uses, and/or distribution of the regulated article (e.g., greenhouses, laboratory, or growth chamber location; field trial location; pilot project location; production, propagation, and manufacture location; proposed sale and distribution location);
(12) A detailed description of the proposed procedures, processes, and safeguards which will be

used to prevent escape and dissemination of the regulated article at each of the intended destinations;
(13) A detailed description of any biological material (e.g., culture medium, or host material) accompanying the regulated article during movement; and
(14) A detailed description of the proposed method of final disposition of the regulated article. 7 CFR 340.4(b)

A. Permit Conditions

When a Form 2000 Permit is issued, the handling of the regulated article should be in accordance with the permit conditions.

Permit conditions. A person who is issued a permit and his/her employees or agents shall comply with the following conditions, and any supplemental conditions which shall be listed on the permit, as deemed by the Administrator to be necessary to prevent the dissemination and establishment of plant pests:
(1) The regulated article shall be maintained and disposed of (when necessary) in a manner so as to prevent the dissemination and establishment of plant pests.
(2) All packing material, shipping containers, and any other material accompanying the regulated article shall be treated or disposed of in such a manner so as to prevent the dissemination and establishment of plant pests.
(3) The regulated article shall be kept separate from other organisms, except as specifically allowed in the permit;
(4) The regulated article shall be maintained only in areas and premises specified in the permit;
(5) An inspector shall be allowed access, during regular business hours, to the place where the regulated article is located and to any records relating to the introduction of a regulated article;
(6) The regulated article shall, when possible, be kept identified with a label showing the name of the regulated article, and the date of importation;
(7) The regulated article shall be subject to the application of measures determined by the Administrator to be necessary to prevent the accidental or unauthorized release of the regulated article;
(8) The regulated article shall be subject to the application of remedial measures (including disposal) determined by the Administrator to be necessary to prevent the spread of plant pests;
(9) A person who has been issued a permit shall submit to APHIS a field test report within 6 months after the termination of the field test. A field test report shall include the APHIS reference number, methods of observation, resulting data, and analysis regarding all deleterious effects on plants, nontarget organisms, or the environment.
(10) 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);
(11) A permittee or his/her agent and any person who seeks to import a regulated article into the

United States shall:
(i) Import or offer the regulated article for entry only at a port of entry which is designated by an asterisk in 7 CFR 3 19.37–14(b);
(ii) Notify APHIS promptly upon arrival of any regulated article at a port of entry, of its arrival by such means as a manifest, customs entry document, commercial invoice, waybill, a broker's document, or a notice form provided for such purpose; and
(iii)Mark and identify the regulated article in accordance with § 340.7 of this part. 7 CFR 340.4 (f)

B. What To Submit and Format For Submission

Application for permit. Two copies of a written application for a permit to introduce a regulated article, which may be obtained from APHIS, shall be submitted by the responsible person 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 20737–1 237. If there are portions of the application deemed to contain trade secret or confidential business information (CBI), each page of the application containing such information should be marked “CBI Copy”. In addition, those portions of the application which are deemed “CBI” shall be so designated. The second copy shall have all such CBI deleted and shall be marked on each page of the application where CBI was deleted, “CBI Deleted”. If an application does not contain CBI then the first page of both copies shall be marked “No CBI”. 7 CFR 340.4(a)

C. Confidential Business Information (CBI)

BRS recommends that CBI be minimized especially with regard to confinement protocols, post harvest monitoring procedures and time frames, and methods of disposal. Applicants should submit sufficient non-confidential information so that State reviewers can reasonably assess permit applications. Any articles submitted for publication but not yet published can be submitted and may be claimed as CBI. Guidance for submitting CBI information can be found at (http://www.aphis.usda.gov/brs/pdf/Doc_Prep_Guidance.pdf). Include justification for all material that is claimed as CBI.

D. Permit Amendments

Modifications to a valid (after issuance and prior to expiration) release or movement Form 2000 Permit may be submitted as an amendment. Amendments can be used: to add new genetic constructs, add fields locations within a State already listed on the permit, change disposal methods, change the proposed harvest date of plantings, add an SOP for field equipment and add a contained facility. However, amendments may not be used to: add new States, new recipient organisms, or add new plantings that extend into the next growing season thereby extending the date of the permit. Proposed changes should be described clearly. Include the permit number on all correspondence and follow the instructions for submission of CBI, if applicable. When the permit required the preparation of an EA, additional sites in counties other than those specified in the original permit application may be added providing that the area covered in the EA includes those counties. Send the amendment request to: Permit Specialist, U.S. Department of Agriculture, Animal and Plant Health Inspection Service, BRS, Unit 91, 4700 River Road, Riverdale, MD 20737-1237.

VI. FILLING OUT THE FORM 2000 PERMIT APPLICATION

The following information is provided to assist the applicant in filling out the Form 2000 Permit application Sections 6, 10 and 13. Additional information will be needed when an Environmental Assessment is required. Refer to Section VII on Environmental Assessment.

A. Section 6 - Organism and/or Product

All scientific, common, and trade names, and all designations necessary to identify the: Donor organism(s); recipient organism(s); vector or vector agent(s); constituent of each regulated article which is a product; and, regulated article 7 CFR 340.4 (b)(2)

Provide a detailed description of any biological material such as host material accompanying the regulated article during movement.

B. Section 10 - Location

Include the State(s) and county(s) of release. Neither the States(s) nor the county(s) may be claimed as CBI.

C. Section 13b - Expression

A description of the anticipated or actual expression of the altered genetic material in the regulated article and how that expression differs from the expression in the non-modified parental organism (e.g., morphological or structural characteristics, physiological activities and processes, number of copies of inserted genetic material and the physical state of this material inside the recipient organism (integrated or extrachromosomal), products and secretions, growth characteristics). 7 CFR 340.4 (b)(5)

Provide a detailed description of the gene product including:

- Which of the introduced genes are expressed in the regulated article?
- If the gene product is for therapeutic use, e.g. an antibody or vaccine, provide the type of antibody, IgG, IgM, etc., and epitope or antigen, and the disease and target component of the immune system (e.g. CD8 cells).
- Indicate whether the gene product itself or a down-stream product produced as a result of the gene is the end-use product.
- State whether the transgenic products are new to the plant or are commonly found in plants used for food or feed, or are commonly found in nonplant food sources.

D. Section 13c - Molecular Biology

A detailed description of the molecular biology of the system (e.g., donor-recipient-vector) which is or will be used to produce the regulated article. Country 7 CFR 340.4 (b)(6)

If Agrobacterium was used in the transformation process, indicate if the vector is disarmed (deletion of tumor inducing genes). Describe all new sequences that appear in the regulated article, including promoters, polyadenylation and termination signal sequences, the engineered gene(s), marker or antibiotic resistance gene(s), and other noncoding sequences of known function. Describe the origin of the vector or vector agent which transfers the gene(s) to the recipient. If the vector or vector agent was derived from a plant pest, describe genes that were transferred that are implicated in pathogenicity. Provide a description and origin of all transgenic DNA following this example:

Designation of Transformed Line: VR67
Phenotype Category: 00
Phenotype: Poliovirus vaccine
Construct: pCP 123
Genotype:
Promoter: enhanced 35S 5' from cauliflower mosaic virus (CaMV)
Gene: capsid protein from poliovirus
Enhancer: alcohol dehydrogenase (*adh)* intron 1 from *Zea mays*
Terminator: nopaline synthase (*nos)* 3' from *Agrobacterium tumefaciens* T-DNA
Selectable Marker:
Promoter: 35S 5' from CaMV
Gene: phosphinothricin acetyltransferase (*bar)* from *Streptomyces hygroscopicus* **Terminator:** *nos* 3' from *A. tumefaciens* T-DNA

Use the following Phenotype Category:
AP = Agronomic Properties
BR = Bacteria Resistant
FR = Fungus Resistant
HT = Herbicide Tolerant
IR = Insect Resistant
MG = Marker Genes
NR = Nematode Resistant
OO = Other, may be used for pharmaceutical or industrial intent
PQ = Product Quality
VR = Virus
Resistant

E. Section 13d - Source of Regulated Article

Country and locality where the donor organism, recipient organism, vector or vector agent, and regulated article were collected, developed, and produced. 7 CFR 340.4 (b) (7)

F. Section 13e - Purpose of Introduction and Field Plot Design

A detailed description of the purpose for the introduction of the regulated article including a detailed description of the proposed experimental and/or production design 7 CFR 340.4 (b)(8)

Note: When information is supplied for sections 13e, 13f, and 13h, it is not necessary to repeat information already covered under those items.

Provide a detailed description of the intended use. Indicate whether the regulated article or product will be sold, exported, or moved interstate or intrastate. Include a non-confidential description in laymen's language about the intended use. This will be used to prepare a letter to the State Plant Regulatory Official (SPRO). For example: the gene products may be used to treat a human lung disease or a bacterial disease in young farm animals.

Provide a detailed description of the field plot design including: (1) Field Site Location, (2) Distance to Reproductively Compatible Plants, (3) Field Trial Supervisor, (4) Expected Planting Date, (5) Field Plot Design, (6) Agricultural Practices & Field Observations, (7) Expected Test

Conclusion Date.
The field site location should include the County and State in the CBI-deleted version of the permit application, if the exact location of the field test site is CBI.

The field site information should include the address and exact location of the field test site(s). It should also include adjacent land use information such as research field trails for tobacco, food, or feed crops, other adjacent crops, and proximity to residences.

Provide the distance to nearby crops of the same species as the engineered species.

Provide the name, phone number and if available the email contact information of the field trial supervisor.

For the field plot design, indicate the plant line(s) or organism strain(s) that will be released at the field test site. Describe the field plot, including planted and unplanted areas, perimeter fallow zone, border rows and any areas designated to confine the regulated article to the field test site. Describe any irrigation systems used, particularly if irrigation systems flow into adjacent crop lands.

For agricultural practices & field observations, indicate any chemical or other treatments that may be used to control weeds or prevent pest infestations. Describe frequency of planned monitoring activities, including but not limited to pest control, morphology, plant vigor, water and nutrient status, physiological abnormalities, flower initiation, plant disease, insect damage, and damage from invertebrate and vertebrate pests. Describe plans to monitor for animals in the field when there is a possibility for an adverse effect.

G. Section 13f - Description of Processes to Prevent Dissemination

A detailed description of the processes, procedures, and safeguards which have been used or will be used in the country of origin and in the United States to prevent contamination, release, and dissemination in the production of the: donor organism; recipient organism; vector or vector agent; constituent of each regulated article which is a product; and, regulated article. 7 CFR 340.4 (b)(10).

H. Section 13h - Description of Processes to Prevent Dissemination at Each Destination

A detailed description of the proposed procedures, processes, and safeguards which will be used to prevent escape and dissemination of the regulated article at each of the intended destinations. 7 CFR 340 (b)(12)

The regulated article shall be maintained and disposed of (when necessary) in a manner so as to prevent the dissemination and establishment of plant pests. The regulated article shall be kept separate from other organisms, except as specifically allowed in the permit. The regulated article shall be maintained only in areas and premises specified in the permit. The regulated article shall be subject to the application of measures determined by the Administrator to be necessary to prevent the accidental or unauthorized release of the regulated article. 7 CFR § 340.4 (b)

(12), 7 CFR 340.4 (f)(1),(3),(4),(7).

APHIS regulations require that measures be taken to mitigate dissemination of the engineered organism into the environment during movement and while in the receiving facility (laboratory, growth chamber, or greenhouse). The risk mitigation measures include adequate identification, packaging and segregation measures to prevent or minimize mixing, spillage and dissemination of viable transgenic plant material.
Describe in detail: (1) how the regulated article will be transported during the field trial; (2) how the regulated article will be stored in dedicated facilities; (3) how the access to the seed/or other organisms will be restricted to authorized individuals with appropriate training only; and (4) how viable material will be transported prior to processing or disposal. If a regulated article(s) is to be moved interstate (prior to or after the field release), a separate movement Form 2000 Permit application should be submitted.

1. Considerations for Confinement

This section should describe in detail what measures will be taken by the applicant to confine the regulated article. Measures should be taken to reproductively isolate regulated plants from nonregulated reproductively compatible plants that are not part of the confined release. Both the reproductive isolation measures and post-harvest land use restrictions are based on the reproductive biology and seed dormancy characteristics of the species, surrounding land use, and proximity of reproductively compatible plants. Additional mitigation measures may be necessary based on the nature of the introduced trait(s) and are made on a case-by-case basis. The following mitigation measures are examples of factors that should be considered to prevent the regulated articles or their progeny from persisting in the environment.

2. Site Selection

Consider factors of the field test location to best ensure isolation of regulated and the non-regulated species. Survey the surrounding land to determine if the required isolation distance can be maintained from reproductively compatible plants. Consider previous cropping history of the test plot and surrounding land and anticipated cropping patterns. During the period of time when the regulated article is producing pollen, ensure that the surrounding land is maintained to be free of reproductively compatible plants. The required isolation distance is set by APHIS on a case by case basis depending on the environment of the release and the biology of the regulated article. In general, refer to Supplemental Permit Conditions for previously approved field tests http://www.aphis.usda.gov/brs/ph_permits.html, as these will provide an indication of the required isolation distance. Consideration should also be given to movement of equipment between the storage facility and field site so as to minimize the distance and avoid entering other cropped fields. Select a site that can be accessed by inspectors in the subsequent growing seasons to monitor for volunteers. Where marker posts are used to identify the plot perimeter consider a set back from the road so that vehicles do not knock over the marker posts.

3. Gene Flow by Pollen and Seed Dispersal

One of the major issues for plants is dissemination of the regulated article by pollen. The Association of Seed Certifying Agencies (AOSCA) publishes plant isolation requirements for maintaining seed-stock purity. APHIS/BRS considers these requirements as a reasonable

starting point for designing confinement measures for many experiments as long as one takes into consideration the percentages of outcrossing assumed in those isolation distances. Having considered the pollination and fertilization characteristics of the species, do populations of the species, or related wild or cultivated species with which it can interbreed, exist in the vicinity of the field trial or agricultural site? It may be prudent to allow extra distance as a safety measure. APHIS encourages applicants to use a laser range finder when appropriate to ensure that their isolation distances from sexually compatible plants are accurate. APHIS inspectors will be using these devices to verify the distances. Pollen flow may be confined by one or a combination of measures such as: isolation distance, pollen or pollination-proof caging, netting or bagging prior to flowering, border rows to dilute transgenic pollen, flower removal prior to pollination, use of male sterile lines, use of plant growth regulators to block reproductive development, or temporal isolation through dissimilar flowering times. For plants whose seeds are easily disseminated, e.g. by wind, water, and animals, to a propagative environment, reasonable measures should be taken to minimize potential seed dispersal. Examples include preventing seed from spreading in irrigation water by use of screens or levees, isolation from crops of the same type, netting or fencing to discourage access by animals.

4. Recombinant Viruses Associated With Plants

Can the gene(s) that were introduced be transferred out of the engineered organism to other organisms? If the genes can be mobilized out, explain the mechanism and include data, if available, on the frequency and species of organisms that could be potential recipients. Areas to consider include: Is the virus able to establish itself on/in other species in the surrounding environment? To what extent does the virus survive and reproduce on/in the target plant and/or other plant species in the test site and surrounding environment? Are there any effects on soil microorganisms that are beneficial to plants (e.g. Rhizobium and mycorrhizal fungi)? Can the modified genetic traits be transmitted to other viruses in the environment? What methods are used to monitor the environmental impacts, particularly the population of the modified, target, and nontarget organisms? Can the genetically engineered virus be disseminated by wind, water, soil, mobile organism, or other means?

5. Equipment

Provide SOPs for operating and cleaning equipment. Refer to Appendix I on SOPs and sections specifically covering operating and cleaning equipment. State how planting or harvesting equipment will be dedicated to use on the permitted material for the duration of the permit.

6. Site security

Describe security such as fences, proximity of farm manager to the field test site, and border rows.

7. Monitoring During the Field Test

Monitoring is required to ensure that the isolation distance to reproductively compatible plants is maintained for the duration of the field test. If pollination bags are used or plants are not allowed to flower, describe the frequency that the plants will be checked for intact bags or presence of flowers. Any netting or screen that is used as a bird or insect barrier should be similarly monitored. In all instances of monitoring, describe the action, frequency and duration. Monitor for deleterious effects on plants, nontarget organisms, or the environment.

A person who has been issued a permit shall submit to APHIS a field test report within 6 months after the termination of the field test. A field test report 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 CFR 340.4 (f)(9)

8. Monitoring for Volunteers Following the Field Test

Describe how the regulated area will be monitored for volunteers following the field test, including details on the duration of the monitoring period, the frequency of monitoring, how germination of stray seeds and regrowth from residual plant material will be encouraged (e.g. through irrigation), and destruction of volunteers (e.g. through mechanical means or specific herbicide treatment).

9. SOPs and Personnel Training Program

APHIS requires written documents to be submitted with the Form 2000 permit application that describe in detail, step-by-step, how a procedure will be done for the use of certain types of equipment and processes (referred to as Standard Operating Procedures or SOPs) and how personnel will be trained pertaining to the duties for which they are responsible.

APHIS will require cleaning procedures to be submitted and approved to minimize the risk of seed movement by field operations or equipment (movement of seed on tires of tractors, etc.) from the authorized test site. APHIS will require procedures to be submitted and approved for seed cleaning and drying in order to confine the plant material and minimize the risk of seed loss or spillage. 68 FR 11337 – 11340 II. 1. E. & F.

APHIS will require the permittee to implement an approved training program to ensure that personnel are prepared to successfully implement and comply with permit conditions. 68 FR 11337 – 11340 II. 1. G.

SOPs and Personnel Training Program requirements are covered under Appendix I and II, respectively.

10. Dedicated Storage Facilities for Equipment and Regulated Articles

APHIS will require that planters and harvesters be dedicated to use in the permitted test site(s) for the duration of the tests. In addition, while tractors and tillage attachments, such as disks, plows, harrows, and subsoilers, do not have to be dedicated, they must be cleaned in accordance with protocols approved by APHIS (see item II.1 .E below). To ensure the regulated articles are not inadvertently removed from the site, APHIS authorization will be required before the machinery is used elsewhere. APHIS will require the use of dedicated facilities for the storage of equipment and regulated articles for the duration of the field test. Facilities must be cleaned according to APHIS approved protocols prior to general use of the facilities. 68 FR 11337 – 11340 II. 1. C. and D.

Dedicated facilities (locked or secured buildings, bins, or areas, posted as restricted to authorized personnel only) should be used for storage of equipment and regulated articles for the duration of the field test. Before returning these dedicated facilities to general use, they should be cleaned in

accordance with procedures submitted to and approved by APHIS. The permittee should notify APHIS/BRS and the State Plant Regulatory Official at least 21 calendar days in advance of return to general use to allow for APHIS to schedule an inspection to ensure that the facilities have been cleaned appropriately.

11. Perimeter Fallow Zone

APHIS will increase the size of the perimeter fallow zone (not in production) around the field test site from 25 to 50 feet. This measure is designed to ensure that test plants are not inadvertently commingled with plants to be used for food or feed. APHIS currently prohibits the use of the field test site and its perimeter fallow zone to be used to produce food or feed crops during the tests. APHIS increased the size of the perimeter fallow zone around the test site to allow farm machinery to move around the site and yet still prevent physical mixing of the regulated plants with surrounding plants that may be used for food or feed. 68 FR 11337–11340 II. 1. A.

Food or feed crops may be grown in the fallow zone provided the crops are treated as regulated articles and destroyed at or prior to the completion of the field test. The fallow zone crop should be easily distinguished from the neighboring crops to minimize inadvertent harvesting of the fallow zone with the surrounding crop. When the fallow zone is planted with a crop similar to the neighboring crops, the fallow zone should be harvested (and destroyed if a food or feed crop) prior to the harvest of the neighboring crops, to avoid mixing of the neighboring crops with the harvested fallow zone plant material. Any border rows of non-transgenic plants that are reproductively-compatible with the regulated article are considered part of the field test, should not be harvested and used for food or feed. Border rows should be included in volunteer monitoring the subsequent year. When border rows are planted, the perimeter fallow zone should start outside the border rows.

12. Isolation from Reproductively Compatible Plants

The required isolation distance for pharmaceutical and industrial plants to prevent gene movement by pollen is equal to or greater than that used for foundation varietal purity and is set by APHIS on a case by case basis depending on the area of environment of the release and the recipient organism. In general, the Supplemental Permit Conditions for previously approved permits (http://www.aphis.usda.gov/brs/ph_permits.html) will give an indication of the required isolation distance. The isolation distance begins from the outer edge of the transgenic crop and not the outer edge of the border rows.

APHIS will require that there will be no corn grown within 1 mile (5,280 feet) of the field test site throughout the duration of any field test which involves open-pollinated corn. This establishes a physical isolation distance that is eightfold greater than the isolation distance required for the production of foundation seed (660 feet). When pollen flow is controlled by placing bags around the corn tassels, there will be no other corn within 2,640 feet of the field test site, and the pharmaceutical corn must be planted no less than 28 days before or 28 days after any corn growing in a zone extending from 2,640 to 5,280 feet from the field test site, ensuring there is no overlap in anthesis. With the establishment of isolation distances of 1 mile for open-pollinated corn and one-half mile for controlled pollination corn field tests, APHIS will not allow the use of border rows to reduce these isolation distances. APHIS believes that other methods are available and do not pose the difficulties inherent in using border rows. For example, by eliminating the use of border rows/buffer strips, there will be a reduction in the amount of plant

material that must be disposed of after the field test is terminated (border rows are handled the same as the regulated article, as their proximity to the plots make them possible pollen recipients). This should reduce the possibility of inadvertent mixing of regulated articles with nonregulated plant material. 68 FR 11337-11340 II. 2. A. & B.

Open pollinated corn engineered to produce pharmaceutical or industrial compounds require an isolation distance of at least one mile from any other corn. This is 8 times greater than the isolation distance of 660 feet required for production of foundation seed. Controlled pollination corn (i.e. by bagging, or by the use of male steriles when combined with detasseling) requires at least one-half mile separation from other corn, and corn located beyond one-half mile to one mile should be planted at least 28 days before or 28 days after the corn producing pharmaceutical or industrial compounds. In addition, applicants should check every 2 days to ensure bags are secure or tassels are removed.

13. Equipment Cleaning and Dedicated Planting and Harvesting Equipment

This is covered under SOPs, see Appendix I.

14. Post Harvest Monitoring for Volunteer Plants

Volunteers are succeeding generations of the regulated article that may remain in a field test site after a field test is completed. A volunteer monitoring period is generally required to ensure that any viable material remaining at the field test site after the harvest of the regulated article is destroyed. Following the harvest of the field test, all volunteers should be removed from the field test site or destroyed before they flower. The field test site including the perimeter fallow zone should be monitored for the presence of volunteer plants after harvest of the field test according to the time frame in the Supplemental Permit Conditions. The duration of the monitoring period is based on the seed dormancy characteristics, germination and expected survival rates of the regulated article in the specific release environment. For example corn in temperate climates may volunteer typically for only a single growing season. The seed lacks dormancy and generally germinates in the spring or summer following the fall harvest. Thus, the period of monitoring in temperate climates is one year from the date of harvest. In sub-tropical and tropical climates there may be multiple growing cycles. In such climates where growing conditions allow for germination of the seeds year round, the period of monitoring may be reduced as long as the environmental conditions are such that any seeds in the ground would germinate. In such cases, APHIS may request data verifying that the growing conditions support seed germination, by planting seeds in the field test at the time of harvest and documenting germination.

15. Post Harvest Land Use Restrictions

APHIS will restrict the production of food and feed crops at the field test site and perimeter fallow zone in the following season in cases where there is a potential for volunteer plants to be inadvertently harvested with the following crop. 68 FR 11337-11340 II.1.B

Production of food and feed crops at the field test site and the perimeter fallow zone is restricted during the field test and the growing season(s) following harvest of a field test. Authorization in the form of an approved variance should be obtained from APHIS/BRS prior to planting any crop to be used as food or feed at the field test site and perimeter fallow zone during the field test and the post-harvest monitoring period. Requests for such authorization are not encouraged

and will not be granted in cases where there is a potential for plant material derived from, or originating from, the regulated articles to become mixed with the proposed food or feed crop during harvest. Planting of cover crops that will be not be harvested is allowed but should be specified in writing and authorized by APHIS. Such authorization should be requested in the permit application or as a permit amendment. Describe how the cover crop will be destroyed and how domesticated animal grazing will be prevented. When planting a cover crop, pharmaceutical plant volunteers should be readily distinguishable from the cover crop. For example a corn crop should not be followed by sorghum, because immature sorghum plants look similar to immature corn plants.

I. Section 13g – Destination

A detailed description of the intended destination (including final and all intermediate destinations), uses, and/or distribution of the regulated article (e.g., greenhouses, laboratory, or growth chamber location; field trial location; pilot project location; production, propagation, and manufacture location; proposed sale and distribution location). 7 CFR 340.4 (b)(1 1)

J. Section 13i – Devitalization & Disposal

A detailed description of the proposed method of final disposition of the regulated article 7 CFR 340.4 (b)(14)

Provide a detailed description of the proposed method of final disposition of the regulated article. Transgenic plant material should be devitalized and disposed of by suitable means when no longer in use or authorized. Viable material may be stored in a contained facility. If the material is not devitalized, measures should be taken to ensure that the stored regulated material is kept separate from non-regulated material. If the material is devitalized, the means of devitalization and disposal could include, but are not limited to, dry heat, steam heat, crushing, deep burial and/or chemical treatment. Describe the details of the devitalization measures that will be used. The disposal sites for live material that are not part of the release site should be specified.

VII. SUBMISSIONS TO APHIS AFTER THE RELEASE PERMIT IS APPROVED

A. Where to Send Reports and Notices

Send Reports and Notices to BRS by e-mail, mail, or fax to the addresses and phone numbers listed in the Supplemental Permit Conditions. Follow CBI formatting guidelines when submitting CBI reports and include the Form 2000 Permit number.

B. Pre-Planting Notice

At least 7 calendar days before the release, submit a Pre-Planting Notice that includes the following information for each field test site: (1) a map that clearly identifies the site location to facilitate inspections, (2) the proposed date of release, and (3) indicate if planting and harvesting equipment will be moved between authorized field test sites. The map should indicate the field test site, border rows, storage areas, and major nearby geographic features such as waste areas, steep inclines or declines.

C. Planting Report

Submit a Planting Report within 28 calendar days after release of the regulated article (e.g. planting or inoculation) at each location listed in the permit application. When multiple releases occur in one month, one Planting Report may be submitted listing all the releases for that month. If the plantings are spread out over multiple months, a Planting Report should be sent each month that planting occurs. The Planting Report should include for each field test site: (1) the date of the release, (2) the size in acres for each plant line, (3) the size in acres including fallow zones or border areas, (4) the size in acres excluding border rows, (5) the GPS coordinates of at least one corner or center point (when circular), (6) the distance to the nearest reproductively compatible species, (7) distance to the nearest plants of the same crop which will be used for human consumption (i.e. eating, smoking or chewing) or seed production and, (8) a map identifying any changes from the map submitted with the Pre-Planting Notice. If no planting is to occur or it is known that certain sites will not be planted, this information should be communicated in the planting report.

D. Pre-Harvest Notice

Submit a Pre-Harvest Notice at least 21 calendar days prior to the anticipated harvest. The Pre-Harvest Notice should include the planned date of harvest and indicate plans for moving harvesting equipment from the test site. If multiple, partial harvests are planned, only report the first date of planned harvest at each location. Indicate in the report that subsequent harvests will occur over time, and the estimated date of each harvest for the field trial at each location.

E. Field Test Report

Supplemental Permit Conditions will require a Field Test Report to be submitted within 12 months from the date the permit is issued. As the report will be used in the review of subsequent applications, ideally the report should be submitted at or before the time of a relevant subsequent permit release application. The Field Test Report should include: (1) observations of any deleterious effects on plants (for example plants that have increased susceptibility to plant pests or excessive morbidity), non-target organisms, or the environment; (2) unanticipated effects that impact confinement and; (3) State how and when the regulated article was devitalized (If the regulated article such as seeds have not yet been processed, state where the seeds are stored, the amount stored and the anticipated date of devitalization; and (4) any additional data or information requested by APHIS in the Supplemental Permit Conditions.

F. Volunteer Monitoring Report

Submit a Volunteer Monitoring Report within two years from the issuance date. The monitoring area includes the field test site, border row areas and the perimeter fallow zone. The Volunteer Monitoring Report should include: (1) the dates inspected, (2) the number of volunteers observed, (3) dates of destruction and, (4) actions taken to remove or destroy volunteers.

G. Requests for APHIS Authorization to Return to General Use: Dedicated Harvesters, Dedicated Planters or Storage Facilities

Use the contact information found in the Supplemental Permit Conditions to schedule an

inspection to return to general use of dedicated harvesters, planters, or storage facilities before they are returned to general use. Contact APHIS at least 21 days prior to anticipated inspections.

VIII. ENVIRONMENTAL ASSESSMENT

According to APHIS National Environmental Policy Act (NEPA) implementation regulations (7 CFR 372 available at http://www.access.gpo.gov/nara/cfr/waisidx_08/7cfr372_08.html, confined field tests may be categorically excluded from the requirement of conducting an environmental assessment (EA) because the means through which adverse environmental impacts may be avoided or minimized have been built into the confinement and containment actions themselves. However, an EA may be required when a confined field release of genetically engineered organisms or products involves new species, organisms or novel modifications that raise new issues per 7 CFR 372 (d)(4). Since 2004, APHIS has published its decision summary for determination of a categorical exclusion for each pharmaceutical field trial (on the BRS website http://www.aphis.usda.gov/brs/ph_permits.html, under "NEPA document"). If the agency determines that an EA or an EIS must be prepared, additional information may be required from the applicant for this purpose. Refer to Appendix IV for the scope and type of information that will be required for the preparation of an EA or an EIS. As field trials are conducted over several seasons, applicants should collect data that will assist the agency when it is deemed necessary to prepare an environmental document. Information would typically consist of data relating to potential effects on non-target organisms, humans, wildlife, and the environment from exposure resulting from the introduction.

For Topics Covered in an Environmental Assessment and Additional Information Required For An Environmental Assessment, see Appendix IV.

Because of the additional time required to complete an EA, publish the EA in the Federal Register for public comment and address any public comments, permit applications that will require an EA, should be submitted at least 180 days prior to a requested release date.

IX. MOVEMENT PERMIT APPLICATIONS

A. Submitting Interstate or Importation Movement Permit Applications

(1) Limited permit for interstate movement. The responsible person may apply for a single limited permit for the interstate movement of multiple regulated articles in lieu of submitting an application for each individual interstate movement. Each limited permit issued shall be numbered and shall be valid for one year from the date of issuance. If a permit is sought for multiple interstate movements between contained facilities the responsible individual shall specify in the permit application all the regulated articles to be moved interstate; the origins and destinations of all proposed shipments; a detailed description of all the contained facilities where regulated articles will be utilized at destination; and a description of the containers that will be used to transport the regulated articles. A limited permit for interstate movement of a regulated article shall only be valid for the movement of those regulated articles moving between those locations specified in the application. If a person seeks to move regulated articles other than those specified in the application, or to a location other than those listed in the application, a supplemental application shall be submitted to APHIS. No person shall move a regulated article

interstate unless the number of the limited permit appears on the outside of the shipping container. The responsible person shipping a regulated article interstate shall keep records for one year demonstrating that the regulated article arrived at its intended destination. The responsible person seeking a limited permit for interstate movement shall submit on an application form obtained from APHIS, the data required by paragraphs (b) (1), (2), (4), (6), (7), (9), and (11) through (14) of this section. (2) Limited permit for importation. The responsible person seeking a permit for the importation of a regulated article shall submit an application for a permit prior to the importation of each shipment of regulated articles. The responsible person importing a regulated article shall keep records for one year demonstrating that the regulated article arrived at its intended destination. The responsible person seeking a limited permit for importation shall submit on an application form obtained from APHIS data required by paragraphs (b) (1), (2), (4), (6), (7), (9), and (11) through (14) of this section. 7 CFR 340.4 (c)(1), (2)

APHIS regulations require that if a regulated article is transported interstate or imported, a separate Form 2000 Permit Movement application should be submitted. Applicants should fill out all information except 12, 13(a), 13(b), 13(e), and 13(f) of the Form 2000 Permit application, following procedures in this guidance document entitled "Filling Out Form 2000". Toxicological data is not required for movement permit applications. Include a description of the containers that will be used to transport the regulated articles, a detailed description of all the contained facilities where regulated articles will be utilized at destination, and a description of the containers that will be used to transport the regulated articles. Provide the street address and when appropriate, the building room number when the regulated article will be stored. A permit for interstate movement of a regulated article is only valid for the movement of regulated articles moving between those locations specified in the application. The responsible person importing or shipping a regulated article interstate should keep records for one year demonstrating that the regulated article arrived at its intended destination.

B. Importation

When the permit is issued, blue and white labels (APHIS Form 2051) will be provided that will direct the package to the appropriate port of arrival to clear US Customs. Follow the instructions for labeling the package on the blue and white labels and those in 7 CFR 340.7 Marking and Identity. Attach a blue and white label to each package. Failure to follow instructions may result in significant delays or destruction at the port of arrival into the United States. Contact the BRS Permit Specialist for additional questions regarding packaging and package labeling at phone number (301) 734-8231.

C. APHIS PPQ Requirements

Living organisms may also require an APHIS Plant Protection and Quarantine (PPQ) authorization for movement and importation. Contact PPQ to determine if any additional permits are required and for applicable quarantine restrictions http://www.aphis.usda.gov/ppq/permits/plantpest/pathogen.html. There may be situations where PPQ will require a PPQ routing label. This is often the case for importations. Check with the BRS Permit Specialist (301-734-8231) to ensure BRS and PPQ routing labels are to the same port of entry.

D. Renewals

Renewals may receive shorter review. In the case of a renewal for a limited permit for importation that has been issued less than one year earlier, APHIS will notify the responsible person within 15 days that either: (1) The renewal permit is approved or (2) that a 60 day review period is necessary because the conditions of the original permit have changed. 7 CFR 340.4

Permits for importation may be reviewed in a shorter time frame than required the first time an importation is submitted.

E. Container Requirements

7 CFR 340.1 defines movement as: To ship, offer for shipment, offer for entry, import, receive for transportation, carry, or otherwise transport or move, or allow to be moved into, through, or within the United States.

Articles moved under Form 2000 Permit, including those that are destined for export, should be moved according to APHIS regulations detailed in 7 CFR 340.8. If you plan to ship using containers other than those detailed in this regulation, you should request in writing a container variance, for instance if you plan to ship in plastic containers instead of metal containers

F. Container Variances

A responsible person who believes the container requirements normally applicable to the movement of the person's regulated article (7 CFR 340.8) are inappropriate due to unique circumstances (such as the nature, volume, or life stage of the regulated article) may submit a request for a variance from the container requirements. Acceptable variances generally require a minimum of two levels of containment where each level can independently contain the regulated article in the event of a breach of one level of containment. You should describe packaging requirements based on the number or weight of seeds or plant parts, shipping distance and method, construction and capacity of containers, their suitability for the type of plant part being shipped and how they are sealed. Container variance requests may be submitted with the permit application, or requested as a permit variance amendment after the permit issued. The request for a variance under this section should consist of a short statement describing why the normally applicable container requirements are inappropriate for the regulated article which the person proposes to move and what container requirements the person would use in lieu of the normally prescribed container requirements. APHIS will review your request for the Container Variance for adequacy in containment. APHIS will notify the permit responsible party if variance was approved or denied. Container methods that are approved for a Container Variance are assigned a BRS variance number and may be applicable to future permits. If you submit a movement Form 2000 Permit application and you wish to request use of previously approved Container Variance, reference the movement Form 2000 Permit and/or the BRS variance number for which the Container Variance was originally submitted.

G. Preparing Packages for Shipment

Refer to section 7 CFR 340.7 for package marking and identity during shipment.

H. Greenhouse and Laboratory Containment

When conducting research on genetically engineered regulated articles producing pharmaceutical and industrial compounds under containment, APHIS recommends that developers consult National Institutes of Health (NIH) Guidelines "NIH Guidelines for Research Involving Recombinant DNA molecules" at http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html, and "A Practical Guide to Containment Greenhouse Research with Transgenic Plants and Microbes" at http://www.isb.vt.edu/cfdocs/greenhouse_manual.cfm.

X. REPORTING UNAUTHORIZED RELEASES AND UNINTENDED EFFECTS

APHIS shall be notified orally immediately upon discovery and notified in writing within 24 hours in the event of any accidental or unauthorized release of the regulated article. Consult the Supplemental Permit Conditions for the appropriate contact information for reporting accidental or unauthorized release within 24 hours. 7 CFR 340.4(f)(10)(i)

APHIS shall be notified in writing as soon as possible, but within 5 working days, if the regulated article or associated host organism is found to have characteristics substantially different from those listed in the permit application or exhibits any unusual characteristics (excessive mortality or morbidity, or unanticipated effect on non-target organisms). Consult the Supplemental Permit Conditions for method of reporting for unintended effects within 5 working days. 7 CFR 340.4(f)(10)(ii)

Refer to the Supplemental Permit Conditions for contact information for reporting accidental or unauthorized release.

XI. COURTESY PERMIT

(1) Issuance. The Administrator may issue a courtesy permit for the introduction of organisms modified through genetic engineering which are not subject to regulation under this part to facilitate movement when the movement might otherwise be impeded because of the similarity of the organism to other organisms regulated under this part.
(2) Application. A person seeking a courtesy permit shall submit on an application form obtained from APHIS data required by paragraphs (b) (1), (2), and (5) of this section and shall indicate such data is being submitted as a request for a courtesy permit. A person should also include a statement explaining why he or she believes the organism or product does not come within the definition of a regulated article. The application shall be submitted at least 60 days prior to the time the courtesy permit is sought.
(3) Administrative action. APHIS shall complete an initial review within 15 days of the date of receipt of the application. If the application is complete, the responsible individual shall be notified of the date of receipt of the application for purposes of advising the applicant when the 60 day review period commenced. If the application is not complete, the responsible individual will be advised what additional information must be submitted, and shall commence the 60 day review period upon receipt of the additional information, assuming the additional information submitted is adequate. Within 60 days from the date of receipt of a complete application, APHIS will either issue a courtesy permit or advise the responsible individual that a permit is required under paragraph (b) or (c) of this section. 7 CFR 340.4(h)

Courtesy permits are issued to facilitate movement of non-regulated articles. For example, if a Tobacco Mosaic Virus is genetically engineered to produce a pharmaceutical compound is inoculated onto non-regulated tobacco plants, and then the compound is purified from the inoculated tobacco plant using procedures that would eliminate the transgenic Tobacco Mosaic Virus, the purified product would not be subject to regulation under 7 CFR 340. An applicant should supply plant inoculation data validating the claim that the purified product does not contain transgenic Tobacco Mosaic Virus. Following review of the data, APHIS/BRS may issue a courtesy permit to facilitate movement of the engineered product.

XII. INSPECTION AND COMPLIANCE

Premises inspection. An inspector may inspect the site or facility where regulated articles are proposed, pursuant to a permit, to be released into the environment or contained after their interstate movement or importation. Failure to allow the inspection of a premises prior to the issuance of a permit or limited permit shall be grounds for the denial of the permit. 7 CFR 340.4(d)

A. Timing of Inspections

In order to ensure compliance with the regulations, as well as all permit conditions, APHIS will increase the number of field site inspections during the upcoming growing season to correspond with critical times relevant to the confinement measures. Examples might include inspection at the preplanting stage to evaluate the site location; at the planting stage to verify site coordinates and adequate cleaning of planting equipment; at midseason to verify reproduction isolation protocols and distances; at harvest to verify cleaning of equipment and appropriate storage; at post-harvest to verify cleanup at the field site; and for the following growing season, inspections will be timed to ensure that regulated articles do not persist in the environment. For example, a field test may have five inspections during the growing season and two additional inspections postharvest; however APHIS may inspect more frequently in some cases. 68 FR 11337-11340

APHIS Pharmaceutical and Industrial Trial Inspection Policy

APHIS has adopted a risk-based inspection policy for pharmaceutical and industrial field trials. This approach ensures that inspections occur at critical control points in the production cycle of the regulated article involved in the trial to ensure compliance with regulations and permit conditions.

Generally, for most annual crops a total of seven inspections of the site and the regulated article are performed. These inspections usually occur prior to planting, when the crop is planted, during active growth (generally at mid-season), when the crop is harvested, and after the crop has been harvested. Two inspections are conducted at the same site the following season to monitor for volunteer plants.

The timing of perennial plant inspections may be different than that of annual plants depending on the biology of the plant species involved. Generally, sites are inspected prior to planting and at planting. The regulated article is usually inspected during the period when flowering is expected each year while the trial is active. Harvest and post-harvest inspections are performed in the year in which these activities occur. Site inspections are usually performed the year following the

harvest of the plants to ensure regulated articles do not persist in the environment.

B. Records of Confinement Measures

The responsible party for the Form 2000 Permit should maintain records for the duration of the field trial of confinement measures taken to confine the regulated article.

The permittee must, as always, maintain records of activities related to meeting the permitting conditions. APHIS will increase the auditing of the permittee's records to verify that required permit conditions were accomplished. APHIS will continue to require permittees to regularly inspect sites and maintain accurate records that will be available for APHIS auditing. The permittee will be required to record all efforts undertaken to meet the confinement protocols and other permit conditions. Some of this information will be related to agronomic information (i.e., detasselling, pollination time of test crop, pollination time of surrounding crops, etc.). Frequent APHIS audits will enable the Agency to identify any discrepancies and mitigate any potential adverse effects. 68 FR 11337-11340

C. Contingency Plans

You should consider having contingency plans for how you intend to respond to unauthorized releases to prevent further contamination or dissemination. To reduce the likelihood of unintended release permittees are encouraged to implement a quality monitoring system or external third party auditing system.

D. Compliance with APHIS Regulations

After receipt of a Form 2000 Permit application, APHIS reviews the information submitted. If APHIS determines that additional conditions should be imposed to ensure confinement and mitigate risk associated with the proposed release, APHIS may request that additional information be submitted or may request changes in the field test design. The applicant should conduct the field test using all the conditions stipulated in the permit and the Supplemental Permit Conditions. Any regulated article introduced not in compliance with the requirements contained within 7 CFR Part 340 or any of the Standard or Supplemental Permit Conditions, will be subject to the immediate application of such remedial measures or safeguards deemed necessary by an APHIS inspector, to prevent escape of the regulated article. The responsible party may be subject to fines or penalties as authorized by the Plant Protection Act (7 U.S.C. 7701-7772).

E. Compliance Infractions

Any permit which has been issued may be withdrawn by an inspector or the Administrator if he/she determines that the holder thereof has not complied with one or more of the conditions listed on the permit. 7 CFR 340.4 (g)

Failure to comply with permit and supplemental conditions can result in compliance infractions and the applicant can be ordered to take remedial action (7 U.S.C. 7714(b)(1)) if necessary to prevent the spread of plant pests (7 CFR 340.4 (d) (7) according to the Plant Protection Act.

(1) IN GENERAL.-Any person that violates this title, or that forges, counterfeits, or, without authority from the Secretary, uses, alters, defaces, or destroys any certificate, permit, or other

document provided for in this title may, after notice and opportunity for a hearing on the record, be assessed a civil penalty by the Secretary that does not exceed the greater of- (A) $50,000 in the case of any individual (except that the civil penalty may not exceed $1,000 in the case of an initial violation of this title by an individual moving regulated articles not for monetary gain), $250,000 in the case of any other person for each violation, and $500,000 for all violations adjudicated in a single proceeding; or (B) twice the gross gain or gross loss for any violation, forgery, counterfeiting, unauthorized use, defacing, or destruction of a certificate, permit, or other document provided for in this title that results in the person deriving pecuniary gain or causing pecuniary loss to another. (2) FACTORS IN DETERMINING CIVIL PENALTY.-In determining the amount of a civil penalty, the Secretary shall take into account the nature, circumstance, extent, and gravity of the violation or violations and the Secretary may consider, with respect to the violator-(A) ability to pay; (B) effect on ability to continue to do business; (C) any history of prior violations; (D) the degree of culpability; and (E) any other factors the Secretary considers appropriate. (3) SETTLEMENT OF CIVIL PENALTIES.-The Secretary may compromise, modify, or remit, with or without conditions, any civil penalty that may be assessed under this subsection. 7 U.S.C. 7714(b)(1)

In some cases, such as minor infractions where the applicant identifies the action, notifies APHIS immediately, and takes prompt and appropriate remedial action, a formal written APHIS response may not be necessary. In other cases, written warnings are issued. For the most serious infractions, an investigation is conducted by APHIS Investigations and Enforcement Services (IES) and permittees may be fined. The applicant can also be assessed a criminal or civil penalty for failing to comply with the regulations (7 U.S.C. 7734). If necessary, to protect the environment or public health, the transgenic organisms can be subjected to the application of remedial measures (including disposal) if determined by the APHIS Administrator (7 CFR 340.4 (d)(7)). If the owner fails to take such action, USDA can take the action and recover the cost of the action from the owner (7 U.S.C. 7714 (b)(2)). APHIS has qualified personnel located in every State that can inspect field sites for compliance to the performance standards for field testing.

XIII. APHIS CONTACTS

A Biotechnologist within the BRS/Environmental Risk Analysis Division is assigned to each permit applicant and will review all permit applications submitted by this applicant. If you need assistance in completing the Form 2000 permit application is needed, contact the appropriate Biotechnologist. If a Biotechnologist has not been assigned or for general questions regarding points detailed within this guidance document, please contact Dr. Neil Hoffman, Director of BRS' Environmental Risk Analysis Division, via e-mail at Neil.E.Hoffman@aphis.usda.gov.

XIV. APPENDICES

APPENDIX I: STANDARD OPERATING PROCEDURES

When planting, harvesting, processing and moving the regulated article, APHIS requires the use of certain types of dedicated equipment along with Standard Operating Procedures (SOPs) for cleaning certain types of equipment or facilities and for certain operations that handle or come into contact with regulated plant material.

Equipment Cleaning

APHIS will require cleaning procedures to be submitted and approved to minimize the risk of seed movement by field operations or equipment (movement of seed on tires of tractors, etc.) from the authorized test site. II. 1. F. APHIS will require procedures to be submitted and approved for seed cleaning and drying in order to confine the plant material and minimize the risk of seed loss or spillage. 68 FR 11337-11340 II. 1. E.

To minimize the risk of seed movement and commingling, equipment used for planting and harvesting, as well as other field equipment (e.g. tractors and tillage attachments, such as disks, plows, harrows, and subsoilers) used at any time from the time of planting through the postharvest monitoring period should be cleaned in accordance with procedures submitted to and approved by APHIS before they are moved off the test site. Equipment used to transport seeds or harvested material should be cleaned prior to loading and after transportation according to procedures submitted to and approved by APHIS. Seed cleaning and drying should be performed in accordance with the procedures submitted to and approved by APHIS to confine the plant material and minimize the risk of seed loss, spillage, or commingling.

Dedicated Planting and Harvesting Equipment

APHIS will require that planters and harvesters be dedicated to use in the permitted test site(s) for the duration of the tests. In addition, while tractors and tillage attachments, such as disks, plows, harrows (a cultivator that pulverizes or smoothes the soil) and subsoilers (deep soil tillers), do not have to be dedicated, they must be cleaned in accordance with protocols approved by APHIS (see item II.1 .E below). To ensure the regulated articles are not inadvertently removed from the site, APHIS authorization will be required before the machinery is used elsewhere. 68 FR 11337-11340 II. 1. C.

To ensure that the regulated article is not inadvertently removed from the site, planting and harvesting equipment should be dedicated for use in the permitted test site only from the time of planting through the end of harvesting. After harvest, permittees will not be required to obtain APHIS authorization to use this equipment on APHIS -permitted sites (same sites or different sites) planted with any permitted crops, with any target protein(s) authorized under permit, in subsequent growing seasons under a new permit or a different permit. Authorization is required from APHIS before this planting and harvesting equipment can be used on sites planted to crops not included under permit. The permittee should notify APHIS/BRS and the State Plant Regulatory Official at least 21 calendar days in advance of inspecting this equipment for this purpose so that APHIS may schedule an inspection to ensure that the equipment has been cleaned. Dedicated equipment may be used on any permitted tests from the same applicant.

Submission of SOPs

Applicants should submit a description of the SOPs with each permit application. Even if APHIS has approved previously-submitted protocols you must submit them with a new application. If any changes or additions have been made to previously approved SOPs, please note this in the new application. Altered SOPs should have a new SOP number. Approval of SOPs will occur before permits will be issued.

Risk categories have been assigned to procedures based on the likelihood with which regulated seed or other plant material could become mixed with non-regulated plant material or for viable material to enter a propagative environment in the absence of appropriate SOPs for cleaning or handling. The risk categories are defined as:

Low risk*
Medium risk**
High risk***
Very high risk****

SOPs are required for five categories of processes or equipment. These are as follows:

*******Harvester and ***Planter.*** Cleaning is required before they are moved off the field test site or moved between authorized field test sites on public roads. This equipment should be dedicated to use on authorized sites. Before they are returned to general use, the permittee should notify APHIS- BRS and the State Plant Regulatory Official at least 21 days in advance of inspection so that APHIS or an APHIS certified inspector may schedule an inspection to witness and verify that the cleaning meets the standard that all regulated material is removed.

*****Storage facilities for seed and equipment used to handle regulated articles.*** Cleaning is required before they are returned to general use. The permittee should notify APHIS-BRS and the State Plant Regulatory Official at least 21 days in advance of inspection so that APHIS or an APHIS-certified inspector may schedule an inspection to witness and verify that the cleaning meets the standard that all regulated material is removed.

*******Seed cleaning, processing, and drying (seed for planting or other purposes) of regulated articles.*** Generally these will be contained within the storage facility and will be inspected when that facility is returned to general use. If any of these operations are to occur in the field, then the SOPs should cover how the material will remain in confinement during the process.

Equipment to off-load, haul, or move seed or harvested material, e.g. ***elevators, conveyers, or augers; **trucks and wagons. Cleaning is required before use and after off-loading or transport of regulated seed or harvested material at an authorized site or location

****Tractors (including attachments for spraying, mowing and tilling).*** Tractors and trucks used in the field test site or fallow zone during the growing period of the regulated article or during the volunteer monitoring period should be cleaned prior to movement out of the field.

SOPS SHOULD INCLUDE INFORMATION ON THE FOLLOWING:

Who performs the operation and their qualifications. The person performing the operation should be trained in the APHIS approved SOPs or be supervised by a person trained in the APHIS approved SOPs.

For cleaning harvesters, planters, augers, elevators, and conveyers, the person performing the operation should be specifically trained in the SOP.

Restricted access or use of the equipment. During the time that equipment is being used for the regulated articles and before it is cleaned to be returned to general use, this equipment should be posted as restricted to authorized personnel only. When not is use, it should be locked or secured to prevent use by unauthorized personnel.

Where and when equipment is to be cleaned. Equipment cleaning should be performed on the field test site, fallow zone, or other regulated area designated in the permit or SOPs. This will ensure containment or recovery of seed or other propagules and monitoring for the volunteers in the event that seed enters a propagative environment. If portable equipment cannot be cleaned within 24 - 48 hours after use, it should be enclosed in a restricted area or stored in a secure facility dedicated to the storage of the regulated article and equipment. If moved from the field to a secured storage area, it should be moved in such a way that the regulated article can not spill or be released in transit. The method of movement should be described in the SOP.

Make, model, type, and serial number of the equipment covered by the SOP. This applies to planting and harvesting equipment, equipment used to off-load, haul, or move seed or harvested material [e.g., elevators, augers, trucks, wagons], and seed drying, processing, or cleaning equipment. If no serial number is available, a permanent tag that provides for unique identification should be attached to the equipment. SOPs should be applicable to the make and model of the equipment.

Reference or source of the SOP. Consult manufacturer's instruction manual for cleaning or operation procedures, or other references from agricultural extension or consulting services on cleaning protocols for identity preservation or seed purity.

Step-by-step methods and materials for cleaning:

Harvesters: All areas where seed or other plant material may dislodge from the harvester during transport from the field test site should be cleaned prior to return to the dedicated storage facility storage or transport to another authorized field test site. In the latter case APHIS should be notified. Transport in an enclosed truck or covered trailer will most likely be required unless the harvester is thoroughly cleaned per an SOP applicable to the make and model of the equipment [e.g. as specified by the manufacturer]. For return to "general use", the harvester cleaning should be witnessed, inspected, and approved by APHIS or an APHIS-certified inspector.

Planters: Seed should be removed from hoppers and all areas used to deliver seed (e.g. hoses, tubes, gears, planting shoes) and areas in which seed could reside. If the equipment is being

moved to another authorized site for use with the same or similar constructs, planter boxes, bins, etc. should be removed or emptied, and the planter cleaned sufficiently to prevent material from falling during transport, or it should be transported in an enclosed truck or trailer. Prior to general use, the planter cleaning should be witnessed, inspected and approved by APHIS or an APHIS-certified inspector. SOPs should be applicable to the make and model of the equipment.

Buildings used to store dedicated equipment or regulated articles. Methods such as brushing, wet or dry vacuuming, high pressure water or steam cleaning, should be sufficient to remove seed or other plant material and crop residue from equipment, surfaces, floors, storage areas, etc. For return to general use, the cleaning should be inspected and approved by APHIS or an APHIS-certified inspector.

Seed (or plant material) storage, processing, and drying equipment. Methods should prevent spillage and commingling of plant material with unregulated plant material. Thorough cleaning, (such as brushing, vacuuming of all areas, followed by high pressure hot water, steam cleaning, or compressed air) is required so that NO regulated article remains.

Trucks or wagons used to haul seed or harvested material should be covered or enclosed during transport, and should be swept, brushed, or sprayed out as necessary to remove all regulated plant material from the interior and exterior (including the wheels) after unloading at an authorized facility.

Tractors and other field equipment. Cleaning should be sufficient to remove seed and other plant material from wheels and attachments before moving off of the test site or authorized areas. Appropriate methods might include brushing, hosing, or high pressure spraying. If spraying equipment is used during the period of viable pollen production by the regulated plants, procedures (e.g. high pressure hot water or steam) need to be taken to assure any pollen adhering to the spraying equipment is removed or devitalized before the equipment is used in a sexually compatible species off the field test site.

Effectiveness of the cleaning method. Cleaning records should be presented for cleaning planters and harvesters, and for other equipment such as grain elevators, augers, conveyers, seed cleaners, seed dryers, and seed processors before they are returned to general use unless it can be demonstrated through inspection that the cleaning meets the standards and tolerances required by APHIS. This may require that the equipment be completely disassembled and observed throughout.

Final disposition of material recovered during cleaning operations. Viable plant material should be destroyed, stored in or returned to facilities, field test sites or other locations authorized in the permit. Non-viable material may be disposed of through appropriate waste disposal methods, depending on the constructs and where the foreign protein is expressed. No recovered plant material may be directed toward food or feed use.

APPENDIX II: PERSONNEL TRAINING PROGRAM

APHIS will require the permittee to implement an approved training program to ensure that personnel are prepared to successfully implement and comply with permit conditions. 68 FR 11337 – 11340 II. 1. G.

Training Programs should be Approved by APHIS

The permit responsible party should implement an APHIS-approved training program for each permit to ensure compliance with Permit Conditions, Supplemental Permit Conditions and Permit Standard Operation Procedures (SOPs). Even if a training program has been approved with a previous permit, you must resubmit the training materials that will be used for that permit should be submitted. If any changes or additions have been made to previously approved training materials, please note this in the new application.

Who Should be Trained and Records of Training

All personnel should be trained or work directly under the supervision of someone who has been trained, using the submitted SOPs that describe the actions that they will carry out. All personnel that handle the regulated article should be aware of the actions that should be taken in case of unintended release. APHIS inspectors will determine if the staff involved in particular operations were trained using the approved program for that operation. Records of who is trained, for what activity, and when they were trained should be maintained on site and available during inspection.

Criteria that APHIS uses to approve training programs

The training program should be applicable to all personnel who manage or perform movement or release activities with the regulated article, outside of a contained environment and those who are responsible for regulatory affairs. Personnel should receive instruction and understand APHIS laws, regulations and policies applicable to the introduction of regulated articles pertaining to the duties for which they are responsible.

Training Should Include

1. The regulations at 7 CFR 340 encompassing the requirements dealing with permits for release, interstate movement, and importation as applicable to the permittee's activities (in particular, including sections 7 CFR 340.4 (a)-(f), 7 CFR 340.7 and 7 CFR 340.8).
2. The FR Notice (68 FR 1 1337-1 1340) on Field Testing of plants Engineered to Produce Pharmaceutical and Industrial Compounds.
3. Sections of the Plant Protection Act [7 U.S.C. 7734 (Sec. 424)] and APHIS regulations [7 CFR 340.0 (b), 340.4 (f) (7) and 340.4 (f) (8)] that deal with consequences of noncompliance.

APPENDIX III: SAMPLE THREATENED AND ENDANGERED SPECIES WORKSHEET

RECIPIENT ORGANISM: Tobacco mosaic virus in tobacco

PRODUCT: Alpha galactosidase is produced in TMV infected tobacco tissue. Alpha galactosidase is an enzyme used for the treatment of Fabry's disease. This serious heritable disease arises from a genetic deficiency in the gene for alpha galactosidase.

LOCATION OF FIELD TEST FIELD TRIAL PROCEDURES: Land used for agriculture for more than two decades. Although plants will be topped (flowers removed), an occasional flower may be produced between required inspections of the field by company employees. Leaves will be harvested six to eight weeks after infection and plants will be allowed to regenerate and leaves harvested six to eight weeks later. The nearest nonagricultural water, excluding farm "ponds" is more than one mile from the field site.
Routine agricultural practices will be performed.
Nearest tobacco field is 1/2 mile from the field site.

LEVELS PRODUCED AND TISSUE: One mg of enzyme per gram fresh weight of leaves (greenhouse grown plants). Levels detected in field are lower since plants are more stressed. Less than 0.0 1mg of enzyme per gram fresh weight is detected in roots, pollen, and stems.

ASSESSMENT

Based on literature review and discussion with tobacco scientists, we can identify no organisms, except plant pests and possibly skunks, that consume tobacco tissues. Earthworms are negatively impacted by nicotine production in the soil. Even though tobacco is mainly insect pollinated, a significant impact on pollinator species is not expected because very significant adverse effects are expected from the pesticides which will be applied to control tobacco pests and these will dwarf any effects of the transgenic protein which is not known to be toxic to pollinator species and is poorly expressed in pollen. Tobacco is not sexually compatible with any Threatened and Endangered Species (TES) plant. Any unexpected effects from a field test would be minimal by virtue of being confined to the area within the field site (about five acres per plot; six sites per year).

CONCLUSION: Since there is no identifiable direct effect of this field test on any wild plant or animal species, there is no adverse effect to any threatened or endangered species.

TES SPECIES LIST FROM: KENTUCKY

http://ecos.fws.gov/servlet/TESS WebpageUsa Lists?state=KY accessed March 10, 2003

Number of Animals-38
Status Listing
E Bat, gray (*Myotis grisescens)*
E Bat, Indiana (*Myotis sodalis)*

E Bat, Virginia big-eared (*Corynorhinus (=Plecotus) townsendii virginianus)*
E Bean, Cumberland (pearlymussel) Entire Range; except where listed as Experimental Populations (*Villosa trabalis)*
XN Bean, Cumberland (pearlymussel) AL; Free-Flowing Reach of the Tennessee River below the Wilson Dam, Colbert and Lauderdale Counties, AL (*Villosa trabalis)*
E Blossom, tubercied (pearlymussel) Entire Range; except where listed as Experimental Populations (*Epioblasma torulosa torulosa)*
XN Blossom, tubercled (pearlymussel) AL; Free-Flowing Reach of the Tennessee River below the Wilson Dam, Colbert and Lauderdale Counties, AL (*Epioblasma torulosa torulosa)*
E Catspaw (=purple cat's paw pearlymussel) Entire Range; except where listed as Experimental Populations (*Epioblasma obliquata obliquata)*
XN Catspaw (=purple cat's paw pearlymussel) AL; Free-Flowing Reach of the Tennessee River below the Wilson Dam, Colbert and Lauderdale Counties, AL (Epioblasma obliquata obliquata)
E Clubshell Entire Range; except where listed as Experimental Populations (Pleurobema clava) B Combshell, Cumberlandian Entire Range; except where listed as Experimental Populations (Epioblasma brevidens)
XN Combshell, Cumberlandian AL; Free-Flowing Reach of the Tennessee River below the Wilson Dam, Colbert and Lauderdale Counties, AL (Epioblasma brevidens)
T Dace, blackside (Phoxinus cumberlandensis)
E Darter, duskytail Entire (Etheostoma percnurum)
E Darter, relict (Etheostoma chienense)
T Eagle, bald (lower 48 States) (Haliaeetus leucocephalus)
E Elktoe, Cumberland (Alasmidonta atropurpurea)
E Fanshell (Cyprogenia stegaria)
E Mapleleaf, winged (mussel) Entire; except where listed as experimental populations (Quadrula fragosa)
E Mucket, pink (pearlymussel) (Lampsilis abrupta)
E Mussel, oyster Entire Range; except where listed as Experimental Populations (Epioblasma capsaeformis)
XN Mussel, oyster AL; Free-Flowing Reach of the Tennessee River below the Wilson Dam, Colbert and Lauderdale Counties, AL (Epioblasma capsaeformis)
E Pearlymussel, cracking Entire Range; except where listed as Experimental Populations (Hemistena lata)
F Pearlymussel, dromedary Entire Range; except where listed as Experimental Populations (Dromus dromas)
E Pearlymussel, littlewing (Pegias fabula)
F Pigtoe, rough (Pleurobema plenum)
E Pimpleback, orangefoot (pearlyrnussel) (Plethobasus cooperianus)
T Plover, piping (except Great Lakes watershed) (Charad.rius melodus)
E Pocketbook, fat (Potamilus capax)
E Puma (=cougar), eastern (Puma (=Felis) concolor couguar)
E Riffleshell, northern (Epioblasma torulosa rangiana)
E Riffleshell, tan (Epioblasma florentina walkeri (=E. walkeri))
E Ring pink (mussel) (Obovaria retusa)
E Shiner, palezone (Notropis albizonatus)
E Shrimp, Kentucky cave (Palaemonias ganteri)

E Sturgeon, pallid (Scaphirhynchus albus)
E Tern, least (interior pop) (Sterna antillarum)
B Wartyback, white (pearlymussel) (Plethobasus cicatricosus)

Number of Plants- 9
Status Listing
T Potato-bean, Price's (Apios priceana)
E Rock-cress, Braun's (Arabis perstellata)
E Sandwort, Cumberland (Arenaria cumberlandensis)
T Rosemary, Cumberland (Conradina verticillata)
T Sunflower, Eggert's (Helianthus eggertii)
T Goldenrod, white-haired (Solidago albopilosa) B Goldenrod, Short's (Solidago shortii) T Spiraea, Virginia (Spiraea virginiana)
B Clover, running buffalo (Trifolium stoloniferum)

APPENDIX IV: ENVIRONMENTAL ASSESSMENT

Topics Covered in an Environmental Assessment

APHIS will request that data are submitted to evaluate potential adverse effects on the environment. A general outline for an EA is as follows:

I. POTENTIAL FOR PERSISTENCE OF THE MODIFIED PLANTS IN THE ENVIRONMENT
II. POTENTIAL FOR GENE TRANSFER
    1. Movement by outcrossing
    2. Movement by animals
    3. Movement of seeds by water
    4. Movement by human error
III. IMPACTS FROM THE USE OF THE MARKER GENE
IV. IMPACT ON NATIVE FLORAL AND FAUNAL COMMUNITIES
    1. Vertebrate Animals
    2. Invertebrate Animals
    3. Aquatic Organisms
    4. Native Floral Communities
V. ALTERATION IN SUSCEPTIBILITY TO DISEASE OR INSECTS
VI. IMPACT ON EXISTING AGRICULTURAL PRACTICES
VII. IMPACT ON ADJACENT ROW CROPS
VIII. FATE OF TRANSGENIC DNA
IX. IMPACTS ON HUMAN HEALTH
X. EFFECTS OF FIELD TEST ON THREATENED AND ENDANGERED SPECIES
XI. CUMULATIVE ENVIRONMENTAL EFFECTS
XII. SPECIAL CONSIDERATIONS: OTHER ENVIRONMENTAL STATUTES AND CONSIDERATIONS

Additional Information Required For an Environmental Assessment

Changes in Amino Acid Sequence

Compare properties of engineered proteins/enzymes with that of the native molecule. Has the cloning procedure, or have you, intentionally altered the amino acid sequence of the protein? What effect, if any, does this change have on the biological properties of the protein?

Level of Product in Plant Parts

Quantify the amount of gene product or if the gene product is an enzyme, provide quantitative enzyme activity in all plant parts (roots, stem, leaves, pollen and seeds). If the product of the enzymatic reaction is important for the intended use, quantify the product. Describe whether the data were obtained from growth chamber-, greenhouse- or field-grown plants.

Natural or Accumulated Toxicants and Impact on Changes in Confinement

Evaluate whether the engineering would be expected to or has altered the levels of any naturally

occurring toxicant in the plant, the accumulation or release of toxic compounds recovered during phytoremediation, or has affected any property that could impact confinement measures like seed dormancy, pollen viability, etc.

Impacts on Non-Target Organisms

If the gene product has toxic activity associated with it, identify the compound(s) and compare gene product levels produced in the engineered plant to naturally occurring levels reported for the non-genetically engineered plant. Address how any differences in levels of substances with known toxic activity will impact non-target organisms especially along relevant exposure routes (i.e., ground water contamination, foraging by native or domestic animals, pollen dispersal via wind). Consider if the engineered organism would have any adverse impacts on associated floral and faunal communities, endangered or threatened organisms, humans, genetic resources (e.g., susceptibility of economically important species to herbicides or pesticides), or agricultural production

Assess if the transgenic product will have direct or indirect adverse effects on non-target organisms including:

1. beneficial organisms (insect pollinators, earthworms, bees, lady beetles, etc.)
2. foraging birds, rabbits, deer, rodents or other wildlife
3. humans (potential problems associated with handling plant or seed material)
4. potential impact on TES, address county- by-county or as appropriate

Impacts on Threatened and Endangered Species (TES)

Submit a TES worksheet using the completed sample worksheet as an example as found in Appendix III. The assessment may be completed for one or more counties or for the entire state. Keep in mind that if the TES worksheet is completed for the entire State, this same worksheet may be used if additional counties are later added, as long as the TES organism list is updated. Lists of TES by State are available at:
http://ecos.fws.gov/tess_public/pub/stateListingAndOccurrence.jsp?state=all
The range, habitat, and diet of the TES should be considered. We strongly encourage that the TES worksheet contain no CBI.