ENVIRONMENTAL PROTECTION AGENCY

[OPP–2003–0165; FRL–7306–4]

Notice of Filing a Pesticide Petition to Establish a Tolerance for a Certain Pesticide Chemical in or on Food

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: This notice announces the initial filing of a pesticide petition proposing the establishment of regulations for residues of an inert ingredient hygromycin B phosphotransferase (APH4) marker protein and the genetic material necessary for its production in or on various food commodities.

DATES: Comments, identified by docket ID number OPP–2003–0165, must be received on or before July 11, 2003.

ADDRESSES: Comments may be submitted electronically, by mail, or through hand delivery/courier. Follow the detailed instructions as provided in Unit I. of the **SUPPLEMENTARY INFORMATION**.

FOR FURTHER INFORMATION CONTACT: Leonard Cole, Biopesticides and Pollution Prevention Division (7511C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001; telephone number: (703) 305–5412; e-mail address: *cole.leonard@epa.gov.*

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. Potentially affected entities may include, but are not limited to:

- Crop production (NAICS 111)
- Animal production (NAICS 112)
- Food manufacturing (NAICS 311)
- Pesticide manufacturing (NAICS 32532)

This listing is not intended to be exhaustive, but rather provides a guide for readers regarding entities likely to be affected by this action. Other types of entities not listed in this unit could also be affected. The North American Industrial Classification System (NAICS) codes have been provided to assist you and others in determining whether this action might apply to certain entities. If you have any questions regarding the applicability of this action to a particular entity, consult the person listed under **FOR FURTHER INFORMATION CONTACT**.

B. How Can I Get Copies of this Document and Other Related Information?

1. *Docket.* EPA has established an official public docket for this action under docket identification (ID) number OPP–2003–0165. The official public docket consists of the documents specifically referenced in this action, any public comments received, and other information related to this action. Although a part of the official docket, the public docket does not include Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. The official public docket is the collection of materials that is available for public viewing at the Public Information and Records Integrity Branch (PIRIB), Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Hwy., Arlington, VA. This docket facility is open from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The docket telephone number is (703) 305–5805.

2. *Electronic access.* You may access this **Federal Register** document electronically through the EPA Internet under the ''**Federal Register**'' listings at *http://www.epa.gov/fedrgstr/*.

An electronic version of the public docket is available through EPA's electronic public docket and comment system, EPA Dockets. You may use EPA Dockets at *http://www.epa.gov/edocket/* to submit or view public comments, access the index listing of the contents of the official public docket, and to access those documents in the public docket that are available electronically. Although not all docket materials may be available electronically, you may still access any of the publicly available docket materials through the docket facility identified in Unit I.B.1. Once in the system, select ''search,'' then key in the appropriate docket ID number.

Certain types of information will not be placed in the EPA Dockets. Information claimed as CBI and other information whose disclosure is restricted by statute, which is not included in the official public docket, will not be available for public viewing in EPA's electronic public docket. EPA's policy is that copyrighted material will not be placed in EPA's electronic public docket but will be available only in printed, paper form in the official public docket. To the extent feasible, publicly available docket materials will be made available in EPA's electronic public docket. When a document is selected from the index list in EPA Dockets, the system will identify whether the document is available for viewing in EPA's electronic public docket. Although not all docket materials may be available electronically, you may still access any of the publicly available docket materials through the docket facility identified in Unit I.B.1. EPA intends to work towards providing electronic access to all of the publicly available docket materials through EPA's electronic public docket.

For public commenters, it is important to note that EPA's policy is that public comments, whether submitted electronically or in paper, will be made available for public viewing in EPA's electronic public docket as EPA receives them and without change, unless the comment contains copyrighted material, CBI, or other information whose disclosure is restricted by statute. When EPA identifies a comment containing copyrighted material, EPA will provide a reference to that material in the version of the comment that is placed in EPA's electronic public docket. The entire printed comment, including the copyrighted material, will be available in the public docket.

Public comments submitted on computer disks that are mailed or delivered to the docket will be transferred to EPA's electronic public docket. Public comments that are mailed or delivered to the docket will be scanned and placed in EPA's electronic public docket. Where practical, physical objects will be photographed, and the photograph will be placed in EPA's electronic public docket along with a brief description written by the docket staff.

C. How and to Whom Do I Submit Comments?

You may submit comments electronically, by mail, or through hand delivery/courier. To ensure proper receipt by EPA, identify the appropriate docket ID number in the subject line on the first page of your comment. Please ensure that your comments are submitted within the specified comment period. Comments received after the close of the comment period will be marked ''late.'' EPA is not required to consider these late comments. If you wish to submit CBI or information that is otherwise protected by statute, please follow the instructions in Unit I.D. Do not use EPA Dockets or e-mail to submit CBI or information protected by statute.

1. *Electronically.* If you submit an electronic comment as prescribed in this unit, EPA recommends that you include your name, mailing address, and an e-mail address or other contact information in the body of your

comment. Also include this contact information on the outside of any disk or CD ROM you submit, and in any cover letter accompanying the disk or CD ROM. This ensures that you can be identified as the submitter of the comment and allows EPA to contact you in case EPA cannot read your comment due to technical difficulties or needs further information on the substance of your comment. EPA's policy is that EPA will not edit your comment, and any identifying or contact information provided in the body of a comment will be included as part of the comment that is placed in the official public docket, and made available in EPA's electronic public docket. If EPA cannot read your comment due to technical difficulties and cannot contact you for clarification, EPA may not be able to consider your comment.

i. *EPA Dockets.* Your use of EPA's electronic public docket to submit comments to EPA electronically is EPA's preferred method for receiving comments. Go directly to EPA Dockets at *http://www.epa.gov/edocket*, and follow the online instructions for submitting comments. Once in the system, select ''search,'' and then key in docket ID number OPP–2003–0165. The system is an ''anonymous access'' system, which means EPA will not know your identity, e-mail address, or other contact information unless you provide it in the body of your comment.

ii. *E-mail.* Comments may be sent by e-mail to *opp-docket@epa.gov*, Attention: Docket ID Number OPP–2003–0165. In contrast to EPA's electronic public docket, EPA's e-mail system is not an ''anonymous access'' system. If you send an e-mail comment directly to the docket without going through EPA's electronic public docket, EPA's e-mail system automatically captures your e-mail address. E-mail addresses that are automatically captured by EPA's e-mail system are included as part of the comment that is placed in the official public docket, and made available in EPA's electronic public docket.

iii. *Disk or CD ROM.* You may submit comments on a disk or CD ROM that you mail to the mailing address identified in Unit I.C.2. These electronic submissions will be accepted in WordPerfect or ASCII file format. Avoid the use of special characters and any form of encryption.

2. *By mail.* Send your comments to: Public Information and Records Integrity Branch (PIRIB) (7502C), Office of Pesticide Programs (OPP), Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001, Attention: Docket ID Number OPP–2003–0165.

3. *By hand delivery or courier.* Deliver your comments to: Public Information and Records Integrity Branch (PIRIB), Office of Pesticide Programs (OPP), Environmental Protection Agency, Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Hwy., Arlington, VA, Attention: Docket ID Number OPP–2003–0165. Such deliveries are only accepted during the docket's normal hours of operation as identified in Unit I.B.1.

D. How Should I Submit CBI to the Agency?

Do not submit information that you consider to be CBI electronically through EPA's electronic public docket or by e-mail. You may claim information that you submit to EPA as CBI by marking any part or all of that information as CBI (if you submit CBI on disk or CD ROM, mark the outside of the disk or CD ROM as CBI and then identify electronically within the disk or CD ROM the specific information that is CBI). Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2.

In addition to one complete version of the comment that includes any information claimed as CBI, a copy of the comment that does not contain the information claimed as CBI must be submitted for inclusion in the public docket and EPA's electronic public docket. If you submit the copy that does not contain CBI on disk or CD ROM, mark the outside of the disk or CD ROM clearly that it does not contain CBI. Information not marked as CBI will be included in the public docket and EPA's electronic public docket without prior notice. If you have any questions about CBI or the procedures for claiming CBI, please consult the person listed under **FOR FURTHER INFORMATION CONTACT**.

E. What Should I Consider as I Prepare My Comments for EPA?

You may find the following suggestions helpful for preparing your comments:

1. Explain your views as clearly as possible.

2. Describe any assumptions that you used.

3. Provide copies of any technical information and/or data you used that support your views.

4. If you estimate potential burden or costs, explain how you arrived at the estimate that you provide.

5. Provide specific examples to illustrate your concerns.

6. Make sure to submit your comments by the deadline in this notice.

7. To ensure proper receipt by EPA, be sure to identify the docket ID number assigned to this action in the subject line on the first page of your response. You may also provide the name, date, and **Federal Register** citation.

II. What Action is the Agency Taking?

EPA has received a pesticide petition as follows proposing the establishment and/or amendment of regulations for residues of a certain pesticide chemical in or on various food commodities under section 408 of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a. EPA has determined that this petition contains data or information regarding the elements set forth in FFDCA section 408(d)(2); however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data support granting of the petition. Additional data may be needed before EPA rules on the petition.

List of Subjects

Environmental protection, Agricultural commodities, Feed additives, Food additives, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: May 29, 2003.

Janet L. Andersen,

Director, Biopesticides and Pollution Prevention Division, Office of Pesticide Programs.

Summary of Petition

The petitioner summary of the pesticide petition is printed below as required by FFDCA section 408(d)(3). The summary of the petition was prepared by the petitioner and represents the view of the petitioner. The petition summary announces the availability of a description of the analytical methods available to EPA for the detection and measurement of the pesticide chemical residues or an explanation of why no such method is needed.

Syngenta Seeds, Inc.

PP 3G6590

EPA has received pesticide petition (PP 3G6590) from Syngenta Seeds, Inc., P.O. Box 12257, 3054 Cornwallis Road, Research Triangle Park, NC 27709–2257, proposing pursuant to section 408(d) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a(d), to amend 40 CFR part 180 to establish an exemption from the requirement of a tolerance for the plant-pesticide inert ingredient hygromycin B phosphotransferase (APH4) marker protein and the genetic material

necessary for its production in or on cotton.

Pursuant to section 408(d)(2)(A)(i) of the FFDCA, as amended, Syngenta Seeds, Inc. has submitted the following summary of information, data, and arguments in support of their pesticide petition. This summary was prepared by Syngenta Seeds, Inc. and EPA has not fully evaluated the merits of the pesticide petition. The summary may have been edited by EPA if the terminology used was unclear, the summary contained extraneous material, or the summary unintentionally made the reader conclude that the findings reflected EPA's position and not the position of the petitioner.

A. Product Name and Proposed Use Practices

Hygromycin B phosphotransferase (APH4) marker protein is proposed for use as a plant-incorporated protectant formulation inert ingredient. APH4 protein is an aminocyclitol phosphotransferase that catalyzes the phosphorylation of hygromycin and closely related aminoglycoside antibiotics. Expression of the APH4 gene in plant cells allows for growth and selection of transformed cells in the presence of hygromycin B. APH4 has no insecticidal activity.

B. Product Identity/Chemistry

1. *Identity of the pesticide and corresponding residues.* The *aph4* gene in event COT102 cotton plants was derived from a plasmid harbored by a hygromycin-resistant isolate of *E. coli*, and encodes a 341 amino-acid enzyme, hygromycin B phosphotransferase (APH4). Hygromycin B phosphotransferases with significant homology to the APH4 protein in event COT102 plants have also been identified in other microbes including *Streptomyces hygroscopicus*, the source of hygromycin B.

APH4 has a molecular weight of ca. 42,000 and catalyzes the phosphorylation of the 4-hydroxyl group on the hyosamine moiety of hygromycin B, thereby inactivating it. The enzyme has a narrow range of substrates, in that it phosphorylates hygromycin B, hygromycin B_2 and the closely related antibiotics destomycin A and destomycin B, but does not phosphorylate other aminocyclitol or aminoglycoside antibiotics including neomycin, streptomycin, gentamicin, kanamycin, spectinomycin, tobramycin, and amikacin. Hygromycin B is not used in human clinical therapy, but is principally used as an antihelminthic agent in swine and poultry feeds.

2. *Magnitude of residue at the time of harvest and method used to determine the residue.* A determination of the magnitude of residue at harvest is not required for residues exempt from tolerances. However, the petitioner has provided data on the quantity of APH4 protein measured in various plant parts including seeds of VIP3A cotton, as measured by enzyme linked immunosorbent assay (ELISA). APH4 was either not detectable in most COT102 plant tissues or the levels were too low to quantify. Pollen was the only tissue in which quantifiable levels were measured.

3. *A statement of why an analytical method for detecting and measuring the levels of the pesticide residue are not needed.* An analytical method is not required because this petition requests an exemption from tolerances. However, the petitioner has submitted an analytical method for detection of the APH4 protein by ELISA analysis.

C. Mammalian Toxicological Profile

Syngenta Seeds is providing the results of a mammalian toxicology study, *in vitro* digestibility study, and bioinformatics evaluations conducted on the selectable marker protein APH4. These studies, summarized herein, demonstrate the lack of toxicity of the APH4 protein following acute oral exposure to mice, rapid degradation of APH4 upon exposure to simulated gastric and intestinal fluids, and the lack of amino acid sequence similarity of the APH4 protein to proteins known to be mammalian toxins or human allergens.

When proteins are toxic, they are known to act via acute mechanisms and at very low doses (Ref. 1). Therefore, when a protein demonstrates no acute oral toxicity in high-dose testing using a standard laboratory mammalian test species, this supports the determination that the protein will be non-toxic to humans and other mammals, and will not present a hazard under any realistic exposure scenario, including long-term exposures.

Because it is not possible to extract sufficient APH4 protein from transformed plants for toxicology studies, APH4 protein was produced in recombinant *E. coli* by over-expressing the same *aph4* gene that was introduced into VIP3A cotton event COT102. The *aph4* gene was cloned into the inducible, over-expression pET-3a® vector (Novagen, Madison, WI) in *E. coli* BL21DE3pLysS. The APH4 protein, as encoded in this vector, was identical in amino acid sequence to that encoded by the plant transformation vector, pCOT1, except for an additional 11 amino acids from the T7 Tag™ and three amino acids from the vector polylinker. Following purification from *E. coli*, dialysis and lyophilization, the resulting sample, designated Test Substance APH4-0102, was estimated by ELISA to contain ca. 42.6% APH4 protein by weight. The test material was confirmed to be enzymatically active.

An acute mouse oral toxicity study was conducted at the Syngenta Central Toxicology Laboratory (Alderley Park, Macclesfield, Cheshire, UK) according to OPPTS Harmonized Guideline 870.1100. Test substance APH4-0102 (see above description of test substance) was administered to five male and five female mice strain Alderley Park albino mouse (APfCD-1); 8–9 weeks old via a gavage dose of 1,828 milligrams/kilogram (mg/kg) body weight. The test substance contained ca. 42.6% APH4 protein by weight. Therefore, the mice received ca. 779 mg APH4/kg body weight. A negative control group (5 mice/sex) concurrently received the dosing vehicle alone, a suspension of 1% methylcellulose, at the same dosing volume as used for the test material mixture. Food was provided ad libitum, except during the ca. 1–hour prior to dosing, when the animals were fasted. Water was provided ad libitum throughout the study. Observations for mortality and clinical/behavioral signs of toxicity were made at least twice on the day of dosing, and at least once daily thereafter for 14 days. Detailed clinical observations were made for each animal at each observation time. Body weights were recorded daily and food consumption was recorded weekly. Surviving animals were euthanized 14 days post dosing and subjected to gross necropsy. Organ weights (brain, liver with gall bladder, kidneys and spleen) were recorded and principal tissues were processed for microscopic examination.

No mortalities occurred during the study, and no clinical signs of toxicity were observed in either the test or control groups. There were no treatment-related effects on body weight, food consumption, or organ weights, nor were any treatment-related effects observed following macroscopic or microscopic examination. APH4–0102 is not acutely toxic to mice. There is no evidence of toxicity of the test substance at 1,828 mg APH4–0102/kg body weight, representing ca. 779 mg APH4 protein/kg body weight. The estimated LD_{50} value for pure APH4 protein in male and female mice is >779 mg/kg body weight, the single dose tested.

The APH4 protein shows no homology to proteins known to be

mammalian toxins or human allergens; is not derived from a source known to produce allergens; is not targeted to a cellular pathway for glycosylation in the plant; and is rapidly degraded upon exposure to simulated gastric and intestinal.

The genetic material necessary for the production of APH4 as an inert ingredient are the nucleic acids (DNA) which comprise genetic material encoding this protein and its regulatory regions. ''Regulatory regions'' are the genetic material that control the expression of the genetic material encoding the protein, such as promoters, terminators, and enhancers. DNA is common to all forms of plant and animal life and the Agency has previously stated that they are not aware of an instance where these nucleic acids have been associated with toxic effects related to their consumption as a component of food. These ubiquitous nucleic acids, as they appear in the subject inert ingredient, have been adequately characterized. Therefore, no mammalian toxicity is anticipated from dietary exposure to the genetic material necessary for the production of the subject inert plant pesticidal ingredient.

D. Aggregate Exposure

1. *Dietary exposure*—i. *Food*. Derivatives of cottonseed (e.g., refined cottonseed oil) and fiber (e.g., linters, which are essentially 100% cellulose) are used in some food products. However, APH4 was not detected in most of the samples of COT102-derived cottonseed analyzed or any of the cotton fiber samples analyzed. In the few cottonseed samples in which APH4 was detectable, the quantities were below the limit of quantification (<137 ng APH4/g fresh wt; <150 ng APH4/g dry wt). It is expected that any trace quantities of APH4 in cottonseed will be eliminated by standard seed processing methods. As demonstrated by the analysis of cottonseed products for VIP3A protein, no VIP3A was detected in refined cottonseed oil from COT102-derived plants, despite the presence of ca. 3 micrograms VIP3A/g seed (fresh or dry wt.). Additionally, no protein of any kind was detected in the same sample of refined cottonseed oil. It can be concluded that APH4, as produced in COT102-derived cotton plants, does not pose a risk of becoming allergenic via food, because there will be no exposure via food. Additionally, the APH4 protein shows no amino acid sequence homology to known allergens; is not derived from a source known to produce allergens; is not targeted to a cellular pathway for glycosylation in the plant; and is rapidly degraded upon exposure to simulated gastric and intestinal.

ii. *Drinking water*. No exposure to the APH4 and the genetic material necessary for its production as an inert ingredient via drinking water are expected. The protein is incorporated into the plant and will therefore not be available to drinking water sources.

2. *Non-dietary exposure*. Non-dietary exposure is not anticipated, due to the proposed use pattern of the product. Exposure via dermal or inhalation routes is unlikely because the inert ingredient is contained within plant cells. However, if exposure were to occur by non-dietary routes, no risk would be expected because the APH4 protein is not toxic to mammals.

E. Cumulative Exposure

Because there is no indication of mammalian toxicity to the APH4 protein, it is reasonable to conclude that there are no cumulative effects for this inert ingredient.

F. Safety Determination

1. *U.S. population*. The lack of mammalian toxicity at high levels of exposure to the APH4 protein demonstrates the safety of the product at levels well above possible maximum exposure levels anticipated via consumption of processed food products produced from VIP3A cotton. Moreover, little to no human dietary exposure to APH4 protein is expected to occur via VIP3A cotton. Due to the lack of toxicity of the APH4 protein and its very low potential for allergenicity, dietary exposure is not anticipated to pose any harm for the U.S. population. No special safety provisions are applicable for consumption patterns or for any population sub-groups.

2. *Infants and children*. Syngenta has evaluated the acute toxicity data generated on APH4, the lack of homology to known allergens or toxins, and the limited exposure to this protein based on the residue profile and limited number of food/feed products resulting from cotton and has determined that there is ample evidence to indicate a reasonable certainty of no harm to infants and children as a result of the use of this product.

G. Effects on the Immune and Endocrine Systems

The inert ingredient APH4 is a protein, derived from sources that are not known to exert an influence on the endocrine or immune systems.

H. Existing Tolerances

The registrant is not aware of any known existing tolerances or exemptions for APH4 and the genetic material necessary for its production as an inert ingredient.

I. International Tolerances

The registrant is not aware that any Codex maximum residue levels exist for the APH4 protein and the genetic material necessary for its production.

J. Reference

1. Sjoblad, R.D., J.T. McClintock and R. Engler (1992) Toxicological considerations for protein components of biological pesticide products. *Regulatory Toxicol. Pharmacol.* 15: 3–9.

[FR Doc 03–14327 Filed 6–10–03; 8:45 am]

BILLING CODE 6560–50–S

ENVIRONMENTAL PROTECTION AGENCY

[OPP–2003–0187; FRL–7311–8]

Experimental Use Permit; Receipt of Application for Use of Aspergillus Flavus NRRL 21882

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: This notice announces receipt of an application 75624-EUP-R from Circle One Global, Inc. requesting an experimental use permit (EUP) for the *Aspergillus flavus* NRRL 21882. The Agency has determined that the application may be of regional and national significance. Therefore, in accordance with 40 CFR 172.11(a), the Agency is soliciting comments on this application.

DATES: Comments, identified by docket ID number OPP–2003–0187, must be received on or before July 11, 2003.

ADDRESSES: Comments may be submitted electronically, by mail, or through hand delivery/courier. Follow the detailed instructions as provided in Unit I. of the **SUPPLEMENTARY INFORMATION**.

FOR FURTHER INFORMATION CONTACT: Shanaz Bacchus, Biopesticides and Pollution Prevention Division (7511C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001; telephone number: (703) 308–8097; e-mail address: bacchus.shanaz@epa.gov.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

This action is directed to the public in general. This action may, however, be