ENVIRONMENTAL PROTECTION AGENCY

[OPP–2003–0309; FRL–7326–1]

Phosphomannose Isomerase and the Genetic Material Necessary for Its Production in All Plants; 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 a certain pesticide chemical in or on various food commodities.

DATES: Comments, identified by docket identification (ID) number OPP–2003–0309, must be received on or before November 21, 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: Mike Mendelsohn, Biopesticides and Pollution Prevention Division (7511C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001; telephone number: (703) 308–8715; e-mail address: *mendelsohn.mike@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 ID number OPP–2003–0309. 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 EPA's 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–2003–0309. 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–2003–0309. 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–2003–0309.

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–2003–0309. 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: October 9, 2003.

Janet L. Andersen,

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

Summary of Petition

The petitioner's 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 3E6748

EPA has received a pesticide petition (PP 3E6748) 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 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-incorporated protectant inert ingredient phosphomannose isomerase (PMI) marker protein and the genetic material

necessary for its production in all plants in or on all food commodities.

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

Phosphomannose isomerase (PMI) and the genetic material necessary for its production is proposed for use as an inert ingredient in plants producing a plant-incorporated protectant active ingredient. Production of PMI in plant cells allows for selection and growth of genetically transformed plant cells in the presence of mannose as the sole or primary carbon source. PMI has no pesticidal activity. Its use allows the identification of plant cells that have successfully acquired the genetic material necessary to produce a plant-incorporated protectant.

B. Product Identity/Chemistry

1. *Identity of the pesticide and corresponding residues.* PMI is a ubiquitous enzyme that catalyzes the reversible interconversion of mannose-6-phosphate and fructose-6-phosphate. No other natural substrates for PMI are known. The *pmi* gene (also known as the *manA* gene) that encodes the PMI enzyme in transformed plants was derived from *E. coli* strain K–12. The gene encodes a 391–amino acid protein with an apparent of molecular weight of *ca.* 45,000. Functionally equivalent PMI enzymes with significant amino acid homology to this PMI protein have been identified among many diverse organisms including other bacteria, plants, fungi, insects, nematodes, mammals, and including humans. Unlike the traditional selectable markers used in plant cell transformation, PMI does not confer resistance to an antibiotic or herbicide.

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 PMI protein measured in various plant parts representing an initial line of transformed corn plants. PMI was detected in grain from these corn plants at *ca.* 1–2 parts per million (ppm) on a dry- or fresh-weight basis, as measured by enzyme-linked immunosorbent assay (ELISA). Average PMI levels measured in chopped whole transformed corn plants were less than or equal to *ca.* 5 ppm on a dry-weight basis and less than or equal to *ca.* 1 ppm on a fresh-weight basis. In silage prepared from the same line of transformed corn plants, no PMI was detectable after 29 days.

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 PMI protein by ELISA.

C. Mammalian Toxicological Profile

Syngenta Seeds, Inc. is providing the results of a mammalian toxicology study, *in vitro* digestibility study, heat stability study and bioinformatics evaluations conducted on the selectable marker protein PMI. These studies, summarized herein, demonstrate the lack of toxicity of the PMI protein following acute oral exposure to mice, rapid degradation of PMI upon exposure to simulated gastric and intestinal fluids, instability of the PMI protein upon heating, and the lack of significant amino acid sequence homology of the PMI 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 (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). 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 feasible to extract sufficient PMI protein from transformed plants for toxicology studies, PMI protein was produced in recombinant *E. coli* by over-expressing the same *pmi* gene that was introduced into transformed corn plants. The PMI protein encoded in this *E. coli* system was identical in amino acid sequence to that encoded in the transformed plants, except for additional *N*-terminal amino acids representing 13 amino acids from the T7 Tag™ and 3 amino acids from the vector polylinker. Following purification from *E. coli*, dialysis and lyophilization, the resulting sample, designated test substance PMI–0198, was estimated by ELISA to contain *ca.* 61% PMI protein by weight. PMI as contained in this test substance was enzymatically active, had the predicted apparent molecular weight, and immunoreacted with anti-PMI antibody. Side-by-side comparisons of PMI in test substance PMI–0198 with PMI extracted from transformed corn plants indicated that the proteins are substantially equivalent, as measured by enzymatic activity, apparent molecular weight, and immuno-crossreactivity with anti-PMI antibody. This justified the use of test substance PMI–0198 in safety studies as a surrogate for PMI as produced in transformed plants.

An acute mouse oral toxicity study was conducted according to EPA Harmonized Test Guideline OPPTS 870.1100. Test substance PMI–0198 was administered to seven male and six female mice *via* a gavage dose of 5,050 milligrams/kilogram body weight (mg/kg bwt), representing *ca.* 3,080 mg of pure PMI protein/kg bwt. A negative control group (six males and five females) concurrently received the dosing vehicle alone, a suspension of 0.5% carboxymethylcellulose, at the same dosing volume used for the test substance mixture. No test substance-related mortalities or clinical signs of toxicity occurred during the study. One male in the control group and two males in the test group died as a result of a perforated esophagus due to dosing error. Gross necropsy of the remaining mice at study termination revealed no observable abnormalities. Body weight, body weight gain, and organ weights (brain, liver, kidneys, and spleen) were comparable in the control and test groups. There was no evidence of toxicity. Accordingly, the lethal dose $(LD)_{50}$ value for PMI–0198 in male and female mice is greater than 5,050 mg/kg bwt, and the LD_{50} value for pure PMI protein is greater than 3,080 mg/kg bwt, the single dose tested.

Extensive bioinformatics searches of public protein data bases revealed that the PMI protein shows no significant amino acid homology to proteins known to be mammalian toxins or known or suspected to be human allergens. Additional information and testing indicate that the PMI protein does not have properties that would suggest it has the potential to become a food allergen. The source of PMI (*E. coli*) is not known to produce allergens. Unlike

allergenic proteins, which typically are present at 1–80% of the total protein in an offending food, the average PMI concentration measured in raw grain derived from a line of transformed corn plants represents less than 0.00002% of the total protein. (This calculation is based on corn grain containing 10% total protein by weight, and assumes 2 ppm PMI in the grain.) Additionally, due to degradation *via* food processing methods, PMI will not likely be present in processed food products, or will be present in only trace quantities. PMI produced in transformed plants is not targeted to a cellular pathway for glycosylation. PMI activity, and therefore tertiary protein structure, is lost upon heating at 65 degrees C for 30 minutes. PMI rapidly degrades upon exposure to simulated mammalian gastric and intestinal fluids.

The genetic material occurring in the subject inert ingredient has been adequately characterized. This genetic material (*i.e.*, the nucleic acids deoxyribonucleic acid (DNA) and ribonucleic acid (RNA)), including regulatory regions, necessary for the production of PMI as an inert ingredient in all crops will not present a dietary safety concern. ''Regulatory regions'' are the DNA sequences such as promoters, terminators, and enhancers that control the expression of the genetic material encoding the protein. Based on the ubiquitous occurrence and established safety of nucleic acids in the food supply, a tolerance exemption under the FFDCA regulations has been established for residues of nucleic acids that are part of plant-incorporated protectants or associated inert ingredients 40 CFR 174.475 (66 FR 37817) (FRL–6057–5). Therefore, no mammalian toxicity is anticipated from dietary exposure to the genetic material necessary for the production of PMI protein in all crops.

D. Aggregate Exposure

1. *Dietary exposure*—i. *Food*. Due to the ubiquitous occurrence of PMI in nature, it is conceivable that the human diet has always contained small amounts of PMI proteins that are similar to that produced in plants transformed with the *E. coli pmi* gene. The levels of PMI measured in raw grain from a line of transformed corn plants averaged *ca.* 1–2 ppm. Processed plant products or by-products used in food are unlikely to have measurable PMI protein, or will have only trace amounts. Oral exposure is not expected to result in adverse health effects, because of a demonstrated lack of toxicity to mammals and the rapid digestibility of the PMI protein. It is expected that any PMI protein consumed will be digested as conventional dietary protein.

ii. *Drinking water*. Little to no exposure *via* drinking water is anticipated. Due to the demonstrated mammalian safety profile of PMI, such exposure would not present a risk.

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 PMI protein is not toxic to mammals.

E. Cumulative Exposure

Because there is no indication of mammalian toxicity of the PMI protein or the genetic material necessary for its production, it is reasonable to conclude that there will be 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 PMI protein demonstrates the safety of the product at levels well above possible maximum exposure levels anticipated *via* consumption of food products produced from *pmi*-transformed plants. Moreover, little to no human dietary exposure to PMI protein is expected to occur *via pmi*-transformed food crops. Due to the digestibility and lack of toxicity of the PMI protein, and its very low potential to become an allergen in food, 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*. Based on the mammalian safety profile of the inert ingredient and the proposed use pattern, there is ample evidence to conclude a reasonable certainty of no harm to infants and children.

G. Effects on the Immune and Endocrine Systems

The inert ingredient is 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 PMI 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 PMI protein and the genetic material necessary for its production.

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BILLING CODE 6560–50–S

ENVIRONMENTAL PROTECTION AGENCY

[OPPT–2003–0034; FRL–7331–2]

Draft Instructions for Reporting for the 2006 Partial Updating of the TSCA Chemical Inventory Database; Request for Comment; Notice of Public Meeting

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: EPA is convening a 1–day public meeting to receive comments from persons reporting data required by the Inventory Update Rule (IUR) on the draft instructions for reporting in 2006. The instructions have been revised in response to amendments to 40 CFR part 710 promulgated on January 7, 2003, which substantially modify the information which must be reported for the partial updating of the Toxic Substances Control Act (TSCA) Chemical Inventory Database beginning in 2006.

DATES: The public meeting will commence at 9:30 a.m. on Wednesday, October 22, 2003, and end at approximately 2 p.m.

ADDRESSES: The public meeting will be held at the Sheraton Suites Houston, 2400 West Loop South, Houston, TX 77027.

Persons planning to attend the public meeting are encouraged to register with the technical contact person identified below. Persons registering for the meeting will receive by e-mail a copy of the draft instructions prior to the meeting. Prior registration is not required to attend the public meeting.

FOR FURTHER INFORMATION CONTACT: *For general information contact*: Barbara Cunningham, Director, Environmental Assistance Division (7408M), Office of Pollution Prevention and Toxics, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001; telephone number: (202) 554–1404; e-mail address: *TSCA-Hotline@epa.gov*.

For technical information contact: Fredric C. Arnold, Economics, Exposure, and Technology Division (7406M), Office of Pollution Prevention and Toxics, Environmental Protection Agency, 1200 Pennsylvania Ave., NW.,