

Plant Pesticide Inert Ingredient Phosphinothricin

[Federal Register: August 16, 1995 (Volume 60, Number 158)] [Rules and Regulations]

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ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[PP 4E4410/R2160; FRL-4971-2]

RIN 2070-AB78

Plant Pesticide Inert Ingredient Phosphinothricin Acetyltransferase (PAT) and the Genetic Material Necessary for Its Production (Plasmid Vector pCIBP3064) in Corn; Tolerance Exemption

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This rule establishes an exemption from the requirement of a tolerance for residues of the plant pesticide inert ingredient phosphinothricin acetyltransferase and the genetic material necessary for its production (plasmid vector pCIB3064) in corn. A request for an exemption from the requirement of a tolerance was submitted by the Ciba-Geigy Corp. (Ciba Seed). This regulation eliminates the need to establish a maximum permissible level for residues of this plant pesticide inert ingredient in the raw agricultural commodities of field corn, sweet corn, and popcorn.

EFFECTIVE DATE: Effective on August 16, 1995.

ADDRESSES: Written objections and hearing requests, identified by the document control number [PP 4E4410/R2160], may be submitted to: Hearing Clerk (1900), Environmental Protection Agency, Rm. M3708, 401 M St., SW.,

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Washington, DC 20460. Fees accompanying objections shall be labeled "tolerance Petition Fees" and forwarded to: EPA Headquarters Accounting Operations Branch, OPP (Tolerance Fees) P.O. Box 360277M, Pittsburgh, PA 15251. A copy of any objections and hearing requests filed with the Hearing Clerk should be identified by the document control number and submitted to: Public Response and Program Resources Branch, Field Operations Division (7506C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. In person, bring copy of objections and hearing requests to: Rm. 1132, CM #2, 1921 Jefferson Davis Hwy., Arlington, VA 22202. A copy of objections and hearing requests filed with the Hearing Clerk may also be submitted electronically by sending electronic mail (e-mail) to: opp-docket@epamail.epa.gov. Copies of objections and hearing requests must be submitted as an ASCII file avoiding the use of special characters and any form of encryption. Copies of objections and hearing requests will also be accepted on disks in WordPerfect in 5.1 file format or ASCII file format. All copies of objections and hearing requests in electronic form must be identified by the docket number, [PP 4E4410/R2160]. No Confidential Business Information (CBI) should be submitted through e-mail. Electronic copies of objections and hearing requests on this rule may be filed online at many Federal Depository Libraries. Additional information on electronic submissions can be found below in this document.

FOR FURTHER INFORMATION CONTACT: By mail: Michael L. Mendelsohn, Biopesticides and Pollution Prevention Division, Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. Office location and telephone number: 5th Floor, CS #1, 2800 Crystal Drive, Arlington, VA 22202, Telephone No.: (703)-308-8715; email: mendelsohn.michael@epamail.epa.gov.

SUPPLEMENTARY INFORMATION: EPA issued a notice, published in the Federal Register of

February 1, 1995 (60 FR 6093), which announced that Ciba-Geigy Corp., P.O. Box 12257, Research Triangle Park, NC 27709- 2257, had submitted a pesticide petition (PP) 4E4410 to EPA requesting that the Administrator, pursuant to section 408(d) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a(d), establish an exemption from the requirement of a tolerance for the plant pesticide inert ingredient phosphinothricin acetyltransferase (PAT) as produced in corn by the bar gene and its controlling sequences as found on plasmid vector pCIB3064. EPA has assigned the inert ingredient of this product the name phosphinothricin acetyltransferase and the genetic material necessary for its production (plasmid vector pCIB3064) in corn. "Genetic material necessary for its production" means the genetic materials which comprise genetic material encoding the phosphinothricin acetyltransferase (2) its regulatory regions. "Regulatory regions" are the genetic materials that control the expression of the genetic material encoding the phosphinothricin acetyltransferase, such as promoters, terminators, and enhancers. There were no adverse comments or requests for referral to an advisory committee received in response to the notice of filing of the pesticide petition 4E4410.

Toxicology Assessment

EPA evaluated an acute oral toxicity study and an in vitro digestibility study. In the acute mouse oral toxicity study, a 51PAT protein mixture was shown to have an LD₅₀ greater than 5,050 mg/ kg. The Agency also expects that enzymes with no significant amino acid homology to known protein toxins and which are readily inactivated by heat or mild acidic conditions would also be readily degraded in an in vitro digestibility assay and have little likelihood for displaying oral toxicity. The PAT enzyme meets all the above criteria and, as predicted, submitted data show that no toxicity results when high doses of this protein are administered orally to laboratory rodents. When proteins are toxic, they are known to act via acute mechanisms and at very low dose levels [Sjobald, Roy D., et al., "Toxicological Considerations for Protein Components of Biological Pesticide Products," Regulatory Toxicology and Pharmacology, 15, 3-9 (1992)]. Therefore, since no significant acute effects were observed, even at relatively high dose levels, the PAT protein is not considered acutely or chronically toxic. The PAT acute oral toxicity study together with data indicating that the PAT protein is rapidly degraded in the gastric environment and is also readily denatured by heat or low pH are sufficient to support a finding of no acute mammalian oral toxicity for the PAT protein.

The genetic materials necessary for the production of the PAT protein are the nucleic acids (DNA) which comprise the (1) genetic material encoding the phosphinothricin acetyltransferase and (2) its regulatory regions. "Regulatory regions" are the genetic materials that control the expression of the genetic material encoding the phosphinothricin acetyltransferase, such as promoters, terminators, and enhancers. DNA is common to all forms of plant and animal life, and the Agency knows of no instance where these nucleic acids have been associated with toxic effects related to their consumption. These ubiquitous nucleic acids as they appear in the subject inert ingredient have been adequately characterized by the applicant. Therefore, no mammalian toxicity is expected from dietary exposure to the genetic material necessary for the production of the PAT protein in corn.

Allergenicity

Current scientific knowledge suggests that common food allergens tend to be resistant to degradation by heat, acid, and proteases, are glycosylated and are present at high concentrations in the food. CibaGeigy has submitted data which indicates the PAT protein is rapidly degraded in the gastric environment and is also readily denatured by heat or low pH.

Submitted Data

1. Acute Oral Toxicity of Bacterially Produced PAT Protein. A white powder (PAT-0195) containing 51PAT enzyme by weight was obtained by purification from an E. coli fermentation and dosed at 5,050 mg/kg to mice. No treatment-related significant toxic effects were seen 14 days after oral gavage of high levels of the purified PAT marker protein.
2. In-Vitro Digestibility of PAT Protein. The 22,000 M. W. PAT enzyme is rapidly degraded in the presence of pepsin or low pH so that it loses enzymatic activity and is not detected by SDS-PAGE. The enzyme also loses activity if subject to temperatures over 35 degrees C. EPA was relying on this study to demonstrate rapid degradation of the protein.
3. Acute Oral Toxicity of Corn Leaf Protein Extracted from Bt/PAT Corn. Application of this study to dietary risk assessment is not possible because of extremely low doses administered, small test populations, and the unexplained deaths occurring in both control and treated groups. Therefore,

EPA is not relying on this study to support the tolerance exemption.
Residue Chemistry Data

Residue chemistry data were not required because of the lack of mammalian toxicity of this active

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ingredient. When proteins are toxic, they are known to act via acute mechanisms and at very low dose levels [Sjobald, Roy D., et al. "Toxicological Considerations for Protein Components of Biological Pesticide Products," Regulatory Toxicology and Pharmacology, 15, 3-9 (1992)]. Therefore, since no significant acute effects were observed, even at relatively high dose levels, the PAT protein is not considered acutely or chronically toxic. This is similar to the Agency position regarding toxicity and the requirement of residue data for the microbial *Bacillus thuringiensis* products. [See 40 CFR 158.740(b)] For microbial products, further toxicity testing to verify the observed effects and clarify the source of the effects (Tiers II & III) and residue data are triggered by significant acute effects in studies such as the mouse oral toxicity study.

The genetic material necessary for the production of the PAT protein are the nucleic acids (DNA) which comprise (1) genetic material encoding the phosphinothricin acetyltransferase and (2) its regulatory regions. "Regulatory regions" are the genetic materials that control the expression of the genetic material encoding the phosphinothricin acetyltransferase, such as promoters, terminators, and enhancers. As stated above, no mammalian toxicity is expected from dietary exposure to the genetic material necessary for the production of the PAT protein corn. Therefore, no residue data are required in order to grant an exemption from the requirement of a tolerance for the plant pesticide inert ingredient: phosphinothricin acetyltransferase (PAT) and the genetic material necessary for its production (plasmid vector PCIB3064) in corn.

Conclusions

Based on the information considered, the Agency concludes that establishment of a tolerance is not necessary to protect the public health. Therefore, the exemption from tolerance is established as set forth below.

Any person adversely affected by this regulation may, within 30 days after publication of this document in the Federal Register, file written objections to the regulation and may also request a hearing on those objections. Objections and hearing requests must be filed with the Hearing Clerk, at the address given above (40 CFR 178.20). A copy of the objections and/or hearing requests filed with the Hearing Clerk should be submitted to the OPP docket for this rulemaking. The objections submitted must specify the provisions of the regulation deemed objectionable and the grounds for the objections (40 CFR 178.25). Each objection must be accompanied by the fee prescribed by 40 CFR 180.33(i). If a hearing is requested, the objections must include a statement of the factual issue(s) on which a hearing is requested, the requestor's contentions on such issues, a summary of any evidence relied upon by the objector as well as the other materials required by 40 CFR 178.27. A request for a hearing will be granted if the Administrator determines that the material submitted shows the following: There is genuine and substantial issue of fact; there is reasonable possibility that available evidence identified by the requestor would, if established, resolve one or more of such issues in favor of the requestor, taking into account uncontested claims or facts to the contrary; and resolution of the factual issue(s) in the manner sought by the requestor would be adequate to justify the action requested (40 CFR 178.32).

A record has been established for this rulemaking under docket number [PP 4E4410/R2160] (including objections and hearing requests submitted electronically as described below). A public version of this record, including printed, paper versions of electronic comments, which does not include any information claimed as CBI, is available for inspection from 8 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The public record is located in Room 1132 of the Public Response and Program Resources Branch, Field Operations Division (7506C), Office of Pesticide Programs, Environmental Protection Agency, Crystal Mall #2, 1921 Jefferson Davis Highway, Arlington, VA. Written objections and hearing requests, identified by the document control number [PP 4E4410/R2160], may be submitted to the Hearing Clerk (1900), Environmental Protection Agency, Rm. 3708, 401 M St., SW., Washington, DC 20460.

A copy of electronic objections and hearing requests filed with the Hearing Clerk can be sent directly to EPA at: opp-Docket@epamail.epa.gov

A copy of electronic objections and hearing requests filed with the Hearing Clerk must be

submitted as an ASCII file avoiding the use of special characters and any form of encryption. The official record for this rulemaking, as well as the public version, as described above will be kept in paper form. Accordingly, EPA will transfer any objections and hearing requests received electronically into printed, paper form as they are received and will place the paper copies in the official rulemaking record which will also include all objections and hearing requests submitted directly in writing. The official rulemaking record is the paper record maintained at the address in "ADDRESSES" at the beginning of this document. Under Executive Order 12866 (58 FR 51735, October 4, 1993), the Agency must determine whether the regulatory action is "significant" and therefore subject to all the requirements of the Executive Order (i.e., Regulatory Impact Analysis, review by the Office of Management and Budget (OMB)). Under section 3(f), the order defines "significant" as those actions likely to lead to a rule (1) having an annual effect on the economy of \$100 million or more, or adversely and materially affecting a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local or tribal governments or communities (also known as "economically significant"); (2) creating serious inconsistency or otherwise interfering with an action taken or planned by another agency; (3) materially altering the budgetary impacts of entitlement, grants, user fees, or loan programs; or (4) raising novel legal or policy issues arising out of legal mandates, the President's priorities, or the principles set forth in this Executive Order. Pursuant to the terms of this Executive Order, EPA has determined that this rule is not "significant" and is therefore not subject to OMB review.

Pursuant to the requirements of the Regulatory Flexibility Act (Pub. L. 96-354, 94 Stat. 1164, 5 U.S.C. 601-612), the Administrator has determined that regulations establishing new tolerances or raising tolerance levels or establishing exemptions from tolerance requirements do not have a significant economic impact on a substantial number of small entities. A certification statement to this effect was published in the Federal Register of May 4, 1981 (46 FR 24950).

List of Subjects in 40 CFR Part 180

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: August 7, 1995.

Penelope A. Fenner-Crisp,
Acting Director, Office of Pesticide Programs.

PART 180--[AMENDED]

Therefore, 40 CFR part 180 is amended as follows:

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1. The authority citation for part 180 continues to read as follows:
Authority: 21 U.S.C. 346a and 371.

2. In subpart D, by adding new Sec. 180.1151, to read as follows:

Sec. 180.1151 Phosphinothricin acetyltransferase and the genetic material necessary for its production (plasmid vector pCIB3064) in corn; exemption from the requirement of a tolerance.

Phosphinothricin acetyltransferase and the genetic material necessary for its production (plasmid vector pCIB3064) in corn is exempt from the requirement of a tolerance when used as a plant pesticide inert ingredient in the raw agricultural commodities of field corn, sweet corn, and popcorn. "Genetic material necessary for its production" means the genetic materials which comprise genetic material encoding the phosphinothricin acetyltransferase and its regulatory regions. "Regulatory regions" are the genetic materials that control the expression of the genetic material encoding the phosphinothricin acetyltransferase, such as promoters, terminators, and enhancers.

[FR Doc. 95-20010 Filed 8-15-95; 8:45 am] BILLING CODE 6560-50-F

