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July 17, 2007

Office of Pesticide Programs (OPP)
Regulatory Public Docket (7502P)
Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, D.C. 20460-0001

RE: U.S. Environmental Protection Agency, Exemption Under the Federal Insecticide, Fungicide, and Rodenticide Act for Certain Plant-Incorporated Protectants Derived From Plant Viral Coat Protein Genes(s) Proposed Rule, 72 Fed. Reg. 19590 (Apr. 18, 2007)
Docket ID No. EPA-HQ-OPP-2006-0642

Exemption from the Requirement of a Tolerance under the Federal Food, Drug, and Cosmetic Act for Residues of Plant Virus Coat Proteins that are Part of a Plant-Incorporated Protectant Proposed Rule, 72 Fed. Reg. 19640 (Apr. 18, 2007)
Docket ID No. EPA-HQ-OPP-2006-0643

To whom it may concern:

The Biotechnology Industry Organization (BIO) is pleased to submit these comments in response to the supplemental proposals for plant-incorporated protectants derived from plant viral coat protein genes (PVCP-PIPs) and for plant virus coat proteins (PVC-proteins) that are part of a PIP, published by the U.S. Environmental Protection Agency (EPA or Agency) on April 18, 2007. BIO is a not-for-profit trade association that represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States (U.S.) and in 31 other nations. BIO members are involved in the research and development of healthcare, agricultural, industrial and environmental biotechnology products.

The EPA's authority to adopt exemptions for individual pesticidal substances and categories of pesticidal substances is firmly grounded in the provisions of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug, and Cosmetic Act (FFDCA). The Administrator is authorized to exempt any pesticide from the requirements of FIFRA by regulation if the Administrator finds that the pesticide either is "adequately regulated by another Federal agency" or "of a character which is unnecessary to be subject to this Act in order to carry out the purposes of this Act."[1] Similarly, the Administrator is authorized to establish an

[1] 7 U.S.C. § 136w(b)(2).

exemption from the requirement of a tolerance under the FFDCA for a pesticide chemical residue in or on food if the Administrator determines that the exemption is safe.[2]

BIO supports EPA's proposals to establish science-based exemptions for PVCP-PIPs and PVC-proteins under FIFRA and FFDCA, respectively. As recommended by the National Academy of Sciences, EPA's regulation of PIPs should be considered flexible and open to change so that the Agency can readily adapt to new information and improved understanding of the science that underlies regulatory decisions.[3] EPA has been actively engaged in the regulation of viral coat proteins since 1993, including coat proteins expressed in papaya and squash.[4] The Agency has gained considerable experience with this category of PIPs through these regulatory efforts and as a result of knowledge gained and advice received from six scientific conferences and five meetings of independent, scientific peer review panels, as detailed in the supplemental proposals.[5]

Our specific comments on the current proposals follow.

Coordination with USDA

Under the Coordinated Framework for Regulation of Biotechnology (Coordinated Framework), EPA is the lead agency for regulation of pesticidal substances.[6] With the support of the biotechnology industry, EPA has actively regulated pesticidal substances expressed in biotechnology-derived plants for over 15 years and proposed regulations to address the unique characteristics of those substances in 1994. The first set of PIP regulations was finalized in 2001 and codified in Part 174 of title 40, Code of Federal Regulations.[7]

While the safety of pesticidal substances expressed in biotechnology-derived plants is regulated exclusively by EPA, the safety of biotechnology-derived plants, including those intended to express PIPs, is actively regulated by U.S. Department of Agriculture (USDA) under the Plant Protection Act (PPA).[8] USDA administers a permit program that requires review of the potential agricultural and environmental effects of biotechnology-derived seed, plants and other regulated articles from the earliest field test or other movement through commercialization.[9] USDA's permits and determinations are also reviewed under the National Environmental Policy Act (NEPA).[10]

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[2] 21 U.S.C. § 346a(c)(2).
[3] National Research Council. 2000. Genetically Modified Pest-Protected Plants: Science and Regulation at 153. National Academy Press, Washington, DC.
[4] *See, e.g.,* 59 *Fed. Reg.* 54824 (Nov. 2, 1994) (establishing an exemption from the requirement of a tolerance for residues of virus coat proteins as expressed in a line of squash developed by the Asgrow Seed Company).
[5] 72 *Fed. Reg.* 19594, 19643.
[6] *See* Office of Science and Technology Policy. Coordinated Framework for Regulation of Biotechnology. 51 *Fed. Reg.* 23302, 23304 (June 26, 1986).
[7] 66 *Fed. Reg.* 37772 (July 19, 2001).
[8] 7 U.S.C. §§ 7701 et seq. Similarly, for food and feed crops, the safety of the whole food produced by a biotechnology-derived plant is reviewed by FDA, where it is subject to regulation under the FFDCA.
[9] *See* 7 C.F.R. pt. 340.
[10] 42 U.S.C. §§ 4321 et seq.

EPA has consistently confirmed that it will not regulate PIP-related plants.[11] This division of responsibility is in keeping with the regulatory scheme set forth in 1986 by the federal government for approval of commercial biotechnology products, which designated USDA's Animal and Plant Health Inspection Service as the lead agency for genetically engineered plants.[12] In that capacity, USDA has actively regulated plants that express PVC-proteins since 1993[13] and, like EPA, has gained considerable familiarity with that category of plants.

EPA acknowledges the potential for duplicative oversight by EPA and USDA with respect to certain issues that may arise in decisions about PVCP-PIPs and commits to work together with USDA to avoid potential duplication and inconsistencies.[14] BIO applauds enhanced coordination between EPA and USDA but urges the EPA to reflect its commitment in the proposed FIFRA regulation itself. The proposed FIFRA rule fails to provide any scientific or legal justification for imposing a parallel review process at EPA, including notice and opportunity for comment, in order to qualify for an Agency-determined exemption when the same product must already go through a comparable review process at USDA that also includes public notice and comment under both the PPA and NEPA.

Recognizing that EPA and USDA both review various factors that could affect agriculture and the environment, such as weediness potential and the characteristics of the genetic material that encodes the pesticidal substance, BIO recommends that a determination of nonregulated status or other commercial authorization by USDA under the PPA should be an independent basis by which a PVCP-PIP qualifies for an exemption under FIFRA. This exemption would not affect EPA's food safety responsibilities under the FFDCA, as the Agency would still have to address any potential safety concerns associated with PVC-proteins that might be present in food or feed, including the eligibility of PVC-proteins under the relevant provisions of the proposed FFDCA exemption regulation.

Status of Previously Authorized Products

BIO recommends that those lines of virus resistant plants such as squash and papaya that have already been reviewed by EPA and USDA and received all necessary clearances for commercialization should be expressly exempt from the requirements of FIFRA. Further, all tolerance exemptions previously issued by EPA for PVC-proteins should remain in full force and effect unless modified or revoked by the Administrator under the appropriate provisions of the FFDCA.[15]

Proposed Exemption Process and Criteria

BIO supports EPA's proposal to provide a self-determination option under which a PVCP-PIP would qualify for exemption under FIFRA in appropriate instances, with other determinations to

[11] In the EPA's own words, it has issued "numerous statements that EPA would not regulate the plant per se, but rather substances within the plant when these were used for pesticidal purposes." 66 *Fed. Reg.* 37781; see, also, 59 *Fed. Reg.* 60496, 60498 (Nov. 23, 1994).
[12] 51 *Fed. Reg.* 23304.
[13] *See, e.g.,* 61 *Fed. Reg.* 48663 (Sept. 16, 1996) (determination of nonregulated status for certain papaya lines developed by Cornell University and the University of Hawaii).
[14] 72 *Fed. Reg.* 19593.
[15] 21 U.S.C. § 346a(d), (e).

be made by the Agency after review of the relevant information provided by the developer. BIO also concurs with EPA's focus on the history of safe use and nontarget exposure for PVC-proteins that are expressed in plants by viral coat protein genes. BIO also supports EPA's longstanding policy that exemptions under FIFRA are not intended to cover those PVCP-PIPs that include proteins significantly different from those that occur naturally.

EPA uses two terms to describe proteins that would qualify for exemption under FIFRA and FFDCA, but only defines one, "virtually unmodified," in the proposed regulations. For clarity, EPA should be consistent and just use the term "virtually unmodified" and not the term "minimally modified". Also, the proposed definitions related to modification could be problematic. EPA would define "unmodified" to mean "having or coding for an amino acid sequence that is identical to an entire coat protein of a naturally occurring plant virus." However, plant virus populations are genetically heterogeneous and have a significant natural variability.[16] Thus the determination of "unmodified" or "virtually unmodified" will depend on the comparator used. If a PVCP-PIP has been modified in a fashion that will not meet the current exemption requirements (e.g., deletion, insertion, or certain amino acid substitutions) and yet the change is within the range of natural variability, it would be difficult to prove that the protein is not derived from the naturally existing virus population. BIO supports broadening the definition of the term "virtually unmodified". The reports of the FIFRA Scientific Advisory Panels from 2004 and 2005 both suggested that "the appropriate comparison is to the range of natural variation in the virus population," and found that "[G]iven the possible range of natural variations for PVC proteins, it would be appropriate to assess whether specific modifications are within natural variation limits of the PVC protein on a case-by-case basis." At a minimum, BIO supports adopting both of the changes to the definition of "virtually unmodified" suggested by EPA in the preamble to the FFDCA proposal,[17] i.e., removing the restriction on cysteine, asparagine, serine and threonine, as well as allowing truncated proteins.

Mitigation Measures

EPA has requested comment on the merits of incorporating the use of biocontainment and bioconfinement techniques into the FIFRA exemption criteria such that PVCP-PIPs deployed in tandem with such measures could be found to meet the weediness criterion. The use of appropriate, science-based containment and confinement measures is a well-established method for addressing potential concerns associated with the development and commercial application of biotechnology-derived plants and other organisms. Accordingly BIO supports incorporation of such measures into the FIFRA exemption citeria.

Low-risk Inerts

EPA has requested comment on the development of an Agency-determined approach for exempting inert ingredients under FIFRA. This would enable EPA to review inert ingredients on a case-by-case basis to determine whether they meet the standard established for inert ingredients in the Part 174 regulations. BIO supports a science-based approach that would allow EPA to ensure that a low-risk PVCP-PIP that otherwise meets the Agency's exemption criteria would

[16] Garcia-Arenal, et al. 2001. "Variability and Genetic Structure of Plant Virus Populations," Annu. Rev. Phytopathol.39:157-86.
[17] 72 *Fed. Reg.* 19647 (cross-referenced in the FIFRA preamble at 72 *Fed. Reg.* 19621).

not require registration under FIFRA solely due to the presence of an inert ingredient that may prove to present a low risk upon review.

Nucleic Acids

EPA indicates that it has no intention to amend the existing exemption from the requirement of a tolerance for nucleic acids. There is no evidence that would call into question the exemption issued by EPA in 2001. Accordingly BIO supports the Agency's determination to leave the exemption unchanged.

Terminology

EPA uses the term "invasive species" in various elements of its FIFRA exemption proposal, although the term is not defined. BIO urges EPA to ensure that its use of this term is consistent with Executive Order 13112 and the relevant publications of the Invasive Species Council established pursuant to that Order.[18]

We appreciate the opportunity to provide comments on these proposed exemptions and look forward to working with EPA in the months ahead.

Sincerely,

Michael J. Phillips, Ph.D
Vice President
Food and Agriculture

[18] 64 *Fed. R eg* 6183 (Feb. 8, 1999)