ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 174

[OPP–300370B; FRL–6760–4]

RIN 2070–AC02

Plant-Incorporated Protectants (Formerly Plant-Pesticides), Supplemental Proposal

AGENCY: Environmental Protection Agency (EPA).

ACTION: Supplemental proposal; notice of data availability.

SUMMARY: EPA solicits additional comment on the exemptions it proposed in 1994 for plant-incorporated protectants. Specifically, EPA solicits comment on two alternative regulatory approaches to plant-incorporated protectants derived from plants sexually compatible with the recipient plant that the Agency is considering in response to comments received on the 1994 proposal. EPA requests comment on the issues raised by commenters in response to EPA's 1994 proposed exemptions for plant-incorporated protectants derived from sexually compatible plants, as well as on any new issues presented by the proposed regulatory alternatives. The Agency is requesting comment on whether a distinction made on the basis of process is appropriate. EPA is also providing notice that it has placed the report issued by the National Academy of Sciences (NAS) entitled ''Genetically Modified Plants: Science and Regulation'' in the dockets for the rulemakings relating to certain proposals on plant-incorporated protectants under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug, and Cosmetic Act (FFDCA). With this supplemental document, EPA has reopened the comment period for these particular 1994 proposals to allow the public an opportunity to comment on the information, analyses, and conclusions in the NAS report pertaining to plant-incorporated protectants that act primarily by affecting the plant or are based on viral coat proteins, as well as on specific questions posed by the Agency.

DATES: Comments, identified by docket control number OPP–300370B, must be received on or before August 20, 2001.

ADDRESSES: Comments may be submitted by mail, electronically, or in person. Please follow the detailed instructions for each method as provided in Unit I. of the **SUPPLEMENTARY INFORMATION**. To ensure proper receipt by EPA, it is imperative that you identify docket control number OPP–300370B in the subject line on the first page of your response.

FOR FURTHER INFORMATION CONTACT: By mail: Phillip Hutton, Biopesticides and Pollution Prevention Division (7511C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460; telephone number: (703) 308–8260; e-mail address: hutton.phil&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 a person or company involved with agricultural biotechnology that may develop and market plant-incorporated protectants. Potentially affected categories and entities may include, but are not limited to:

Categories	NAICS codes	Examples of potentially affected entities
Pesticide manufacturers	32532	Establishments primarily engaged in the formulation and preparation of agricultural and household pest control chemicals
Seed companies	111	Establishments primarily engaged in growing crops, plants, vines, or trees and their seeds
Colleges, universities, and professional schools	611310	Establishments of higher learning which are engaged in development and marketing of plant-incorporated protectants
Establishments involved in research and development in the life sciences	54171	Establishments primarily engaged in conducting research in the physical, engineering, or life sciences, such as agriculture and biotechnology

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 table could also be affected. The North American Industrial Classification System (NAICS) codes are provided to assist you and others in determining whether or not this action might apply to certain entities. To determine whether you or your business may be affected by this action, you should carefully examine the provisions in 40 CFR part 174. If you have 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 Additional Information, Including Copies of this Document and Other Related Documents?

1. *Electronically*. You may obtain electronic copies of this document, and certain other related documents that might be available electronically, from the EPA Internet Home Page at http://www.epa.gov/. To access this document, on the Home Page select ''Laws and Regulations,'' ''Regulations and Proposed Rules,'' and then look up the entry for this document under the ''**Federal Register**—Environmental Documents.'' You can also go directly to the **Federal Register** listings at http://www.epa.gov/fedrgstr/.

2. *In person*. The Agency has established an official record for this action under docket control number OPP–300370B. The official record consists of the documents specifically referenced in this action, any public comments received during an applicable comment period, and other information related to this action, including any information claimed as Confidential Business Information (CBI). This official record includes the documents that are physically located in the docket, as well

as the documents that are referenced in those documents. The public version of the official record does not include any information claimed as CBI. The public version of the official record, which includes printed, paper versions of any electronic comments submitted during an applicable comment period, is available for inspection in the Public Information and Records Integrity Branch (PIRIB), Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Hwy., Arlington, VA, from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The PIRIB telephone number is (703) 305–5805.

C. How and to Whom Do I Submit Comments?

You may submit comments through the mail, in person, or electronically. To ensure proper receipt by EPA, it is imperative that you identify docket control number OPP–300370B in the subject line on the first page of your response.

1. *By mail*. Submit your comments to: Public Information and Records Integrity Branch (PIRIB), Information Resources and Services Division (7502C), Office of Pesticide Programs (OPP), Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460.

2. *In person or by courier*. Deliver your comments to: Public Information and Records Integrity Branch (PIRIB), Information Resources and Services Division (7502C), Office of Pesticide Programs (OPP), Environmental Protection Agency, Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Hwy., Arlington, VA. The PIRIB is open from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The PIRIB telephone number is (703) 305–5805.

3. *Electronically*. You may submit your comments electronically by e-mail to: opp-docket&epa.gov, or you can submit a computer disk as described above. Do not submit any information electronically that you consider to be CBI. Avoid the use of special characters and any form of encryption. Electronic submissions will be accepted in WordPerfect 6.1/8.0 or ASCII file format. All comments in electronic form must be identified by docket control number OPP–300370B. Electronic comments may also be filed online at many Federal Depository Libraries.

D. How Should I Handle CBI that I Want to Submit to the Agency?

Do not submit any information electronically that you consider to be CBI. You may claim information that you submit to EPA in response to this document as CBI by marking any part or all of that information as 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 version of the official record. Information not marked confidential will be included in the public version of the official record 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. Offer alternative ways to improve the proposed rule or collection activity.

7. Make sure to submit your comments by the deadline in this document.

8. To ensure proper receipt by EPA, be sure to identify the docket control 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. Background

A. Statutory Authority

Section 2(u) of FIFRA (7 U.S.C. 136 *et seq.*) defines ''pesticide'' as: ''(1) any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest, (2) any substance or mixture of substances intended for use as a plant regulator, defoliant, or desiccant, and (3) any nitrogen stabilizer . . . '' (7 U.S.C. 136(u)). Under FIFRA section 2(t), the term ''pest'' includes ''(1) any insect, rodent, nematode, fungus, weed, or (2) any other form of terrestrial or aquatic plant or animal life or virus, bacteria, or other microorganism'' with certain exceptions (7 U.S.C. 136(t)).

The substances plants produce for protection against pests are pesticides under the FIFRA definition of pesticide, if humans intend to use these substances for ''preventing, destroying, repelling or mitigating any pest,'' regardless of whether the pesticidal capability evolved in the plants, or were introduced through traditional breeding or through the techniques of modern genetic engineering (e.g., recombinant DNA (rDNA)). These substances, produced and used in living plants, along with the genetic material necessary to produce them, are called ''plant-incorporated protectants'' by EPA.

FIFRA section 3 provides, with certain limited exceptions, that no person may sell or distribute in the United States, any pesticide that is not registered under the Act (7 U.S.C. 136a (a)). Before a product may be registered as a pesticide under FIFRA, it must be shown that ''when used in accordance with widespread and commonly recognized practice, it will not generally cause unreasonable adverse effects on the environment'' (7 U.S.C. 136a (c)(5)). A pesticide causes ''unreasonable adverse effects on the environment'' if it causes ''(1) any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide, or (2) a human dietary risk from residues that result from use of a pesticide in or on any food inconsistent with the standard under section 408 of the Federal Food, Drug, and Cosmetic Act. . .'' (7 U.S.C. 136(bb)).

EPA is authorized to promulgate regulations under section 3(a), ''[t]o the extent necessary to prevent unreasonable adverse effects on the environment, [that] limit the distribution, sale, or use in any State of any pesticide that is not registered under this Act and that is not the subject of an experimental use permit under section 5 or an emergency exemption under section 18'' (7 U.S.C. 136a(a)).

A person may, however, sell and distribute an unregistered pesticide if EPA exempts the pesticide pursuant to FIFRA section 25(b)(2). FIFRA section 25(b)(2) authorizes EPA to exempt, by regulation, any pesticide of a character that is unnecessary to be subject to FIFRA in order to carry out the purposes of the Act (7 U.S.C. 136w(b)(2)).

Section 408 of the FFDCA applies to all ''pesticide chemical residues'' which are defined as residues of either a ''pesticide chemical'' or ''any other added substance that is present on or in a commodity or food primarily as a

result of the metabolism or other degradation of a pesticide chemical'' (21 U.S.C. 321(q)(2)). The FFDCA defines ''pesticide chemical'' as: ''any substance that is a pesticide within the meaning of the Federal Insecticide, Fungicide, and Rodenticide Act, including all active and inert ingredients of such pesticide'' (21 U.S.C. 321(q)(1)).

B. Other Federal Agencies

EPA is the Federal agency primarily responsible for the regulation of pesticides. In fulfilling this mission, EPA works closely with the U.S. Department of Agriculture (USDA) which has responsibilities under the Plant Protection Act (PPA), and the U.S. Food and Drug Administration (FDA) which has responsibilities under the FFDCA. EPA, USDA, and FDA consult and exchange information when such consultation is helpful in resolving safety questions. The three agencies also strive for consistency between programs following one of the basic tenets of the Coordinated Framework for Regulation of Biotechnology (51 FR 23302, June 26, 1986); i.e., that the agencies composing the Framework adopt consistent approaches, to the extent permitted by the respective statutory authorities. A consistent approach between agencies is easier for the regulated community to understand. It is also more likely to conserve resources as submitters would more likely be able to use data developed for one agency to meet requirements posed by another agency for the same or similar products.

1. *USDA*. USDA has authority to prevent the introduction and dissemination of plant pests under the PPA. Before introducing into the environment a plant that is regulated under either of these statutes, approval must be obtained from the USDA/Animal Plant Health Inspection Service (APHIS) unless the plant is exempt from USDA/APHIS regulation. The USDA regulations use genetic engineering as a criterion for determining the scope of its regulations (Refs. 1, 2, and 3).

EPA recognizes that there is a potential for duplicative oversight with respect to certain issues that may arise in plant-incorporated protectant decisions. For example, some of the plant-incorporated protectants not exempted by EPA are also subject to APHIS/USDA requirements under the PPA. The potential for most plants containing plant-incorporated protectants to pose weediness concerns is directly considered by USDA/APHIS under PPA. In its reviews of Petitions for Determination of Nonregulated Status under regulations at 7 CFR part 340, the potential for weediness, for displacement of native species, and potential consequences of gene transfer are evaluated by USDA/APHIS. EPA and USDA/APHIS will continue to consult and collaborate when reviews of any plant-incorporated protectant indicates reason for concern over any of these issues. Weediness is generally thought to be due to a multiplicity of factors. The Agencies will work to coordinate their analyses of these factors in accordance with their respective expertise and jurisdiction. EPA's focus in considering these issues is on the statutory determination on unreasonable adverse effects the Agency must make with respect to pesticides, rather than on the engineered plant itself. In particular, these plant-related issues may potentially impact use patterns of pesticides, which are of relevance to the Agency. EPA and USDA/APHIS will work together to avoid potential duplication and inconsistencies.

2. *FDA*. FDA is the primary U.S. agency responsible for ensuring the safety of commercial food and food additives. FDA's authority under FFDCA extends to any nonpesticidal substance that may be introduced into a new plant variety and that is expected to become a component of food. Pursuant to FFDCA and the reorganization that created EPA, pesticides as defined by FIFRA are subject to EPA's regulatory authority under FFDCA. Recently, FDA announced its intent to propose a pre-market notification scheme for foods derived from plants modified through the use of modern biotechnology.

III. Proposed Alternative Regulatory Approaches to Plant-Incorporated Protectants Derived Through Genetic Engineering from Sexually Compatible Plants

In this Unit, EPA describes the two alternative regulatory approaches the Agency is considering to address the issues raised in comment for this class of plant-incorporated protectants. EPA solicits public comment on any new issues presented by the proposed regulatory alternatives as well as on the issues raised in comment on the 1994 proposal. The Agency intends to consider public comments and make final determinations to complete these other rulemakings within 9 to 12 months after the close of the comment period for the supplemental proposal, which is currently set at 30 days. Until the Agency takes a final action on these other exemptions, the Agency intends to maintain its current practices on regulation of plant-incorporated protectants.

A. History

The plant-incorporated protectants that a plant population has evolved, and thus naturally possesses, can be varied, including, for example, structural characteristics of the plant, the production of general metabolites that have toxic properties, biochemical cascades resulting in localized necrosis of plant tissue, or the production of specific toxic substances in response to pest attack. The plant-incorporated protectants that characterize a particular plant population can be shared among the members of the population by the process of sexual hybridization. There is a large base of human experience in selective breeding of plants within sexually compatible populations using conventional hybridization techniques. There is much experience growing such plants, and preparing and consuming food from plants in such populations. Based on this experience and the information base generated through scientific study of such plants and their constituents, and on knowledge in plant genetics, plant physiology, phytopathology, microbial ecology, ecology, plant breeding and biochemistry, EPA proposed in 1994 to exempt plant-incorporated protectants that plants normally possess and are moved between closely related plants. EPA's preferred approach to describing for regulatory purposes this category of plant-incorporated protectants used the criterion of sexual compatibility, including hybridization achieved by wide and bridging crosses.

1. *1994 Proposal*. Plants that are sexually compatible form viable zygotes through the fusion of gametes in sexual hybridization. In the **Federal Register** of November 23, 1994 (59 FR 60519), EPA proposed that plant-pesticides (now plant-incorporated protectants) would be exempt from all FIFRA requirements, except for an adverse effects reporting requirement, if the genetic material that leads to the production of the pesticidal substance is derived from plants that are sexually compatible with the recipient plant and has never been derived from a source that is not sexually compatible with the recipient plant. EPA proposed in 1994 that this exemption for ''sexually compatible'' plant-incorporated protectants would apply regardless of how a plant-incorporated protectant came to be in the plant; e.g., whether they evolved naturally in the plant, or were introduced through traditional breeding or the techniques of genetic engineering, as long as the donor and recipient plant are sexually compatible. EPA's proposal to exempt plant-incorporated protectants from

sexually compatible plants subsumed plant-incorporated protectants in plants propagated vegetatively. In 1994, EPA also published companion proposals under section 408 of the FFDCA that would exempt all residues of plant-incorporated protectants derived from plants sexually compatible with the recipient plant (59 FR 60535, 60542). EPA caveated the 1994 proposals by noting that the Agency did not intend to exempt a plant-incorporated protectant that has been modified so that it is significantly different functionally from the plant-incorporated protectant as it occurs in the source organism (59 FR at 60524). In 1994, EPA also offered for comment two alternative proposed approaches based in whole or in part on taxonomy. All three of these approaches were based on the premise that closely related plants, whether described by sexual compatibility or taxonomy, were unlikely to present novel exposures.

In the 1994 proposals, sexually compatible, when referring to plants, was described as capable of forming a viable zygote through the fusion of two gametes including the use of bridging or wide crosses between plants. Basically this described the traditional breeding techniques of controlled pollination among plants expressing desired traits, seed collection and selection of the resulting progeny for enhanced combinations.

In the 1994 proposals, ''bridging crosses between plants'' were defined as the utilization of an intermediate plant in a cross to produce a viable zygote between the intermediate plant and a first plant, in order to cross the plant resulting from that zygote with a third plant that would not otherwise be able to produce viable zygotes from the fusion of its gametes with those of the first plant. The result of the bridging cross is the mixing of genetic material of the first and third plant through the formation of an intermediate zygote. In the 1994 proposal, ''wide crosses between plants'' would be to facilitate the formation of viable zygotes through the use of surgical alteration of the plant pistil, bud pollination, mentor pollen, immunosuppressants, *in vitro* fertilization, pre- and post-pollination hormone treatments, manipulation of chromosome numbers, embryo culture, or ovary and ovule cultures, or any other technique that the Administrator determines meets this definition.

The Agency also requested in the 1994 **Federal Register**, comment on an exemption criterion based on the process (e.g., rDNA) used to introduce the plant-incorporated protectant into a plant (50 FR at 60514 and 60530). In this approach, plant-incorporated protectants developed through techniques other than those of modern genetic engineering (e.g., rDNA) would be exempted, i.e., those developed through conventional plant breeding would be exempted. Categories of those plant-incorporated protectants that were not exempted could subsequently be considered for exemption on the basis of risk potential. The FIFRA Scientific Advisory Panel (SAP) and the Biotechnology Science Advisory Committee at a joint meeting on January 21, 1994, considered the utility of such an approach, and supported use of a criterion based on rDNA methodologies, based on: the success of the National Institutes of Health Guidelines for Research Involving Recombinant DNA Molecules (e.g., see 59 FR 34496, July 5, 1994); uncertainties about how a gene will function in the new genetic background; and to build public confidence in the products of genetic engineering. The joint meeting report also recommended that further exemptions . . .should be used in conjunction with the criterion based on methodology. The SAP specifically recommended that ''[f]or example, when rDNA methodologies are used to exchange genes between sexually compatible crop plants, the products would be exempt from additional regulation'' (Ref. 4 at 10).

2. *Public comments*. In response to its November 23, 1994 **Federal Register** request for comment on the proposal to exempt plant-incorporated protectants derived from plants sexually compatible with the recipient plant (59 FR at 60533), EPA received 52 comments addressing the issue of scope of exemption. These comments presented a broad range of views. Twenty-seven comments discussed the merits of EPA's 1994 preferred approach; i.e., the exemption proposal based on sexual compatibility between the donor and recipient plants. The majority of these comments favored such an approach, although some commenters favored EPA's alternative proposed approach based in part on taxonomy (Option 3). Others among the 27 comments expressed reservation about the rationale underlying the preferred and alternative approaches, i.e., relatedness among plants being equated to potential for novel exposures. For example, one comment stated that while superficially attractive, EPA's preferred approach was flawed in that it did not consider nontarget exposure by the introduction of a plant into an ecosystem in which it did not evolve.

EPA also received 35 comments on the propriety of relying on the process by which the genetic material is introduced into the plant as a criterion for defining the scope of EPA's regulatory oversight. Twenty of these comments supported an approach based on process, i.e., that those plant-incorporated protectants introduced by rDNA would be regulated, while conventional breeding would be exempt. These comments urged the Agency not to exempt plant-incorporated protectants introduced into the recipient plant by the processes of genetic engineering, regardless of whether they were derived from plants sexually compatible with the recipient plant. The comments focused on a common concern, which can be represented by the following excerpt:

> Genetic engineering (particularly recombinant DNA [rDNA] methodologies), represents a fundamental technical advance over traditional plant breeding in the ability to manipulate plants genetically. . . . given the fact that rDNA technologies represent such a fundamental technical advance over plant breeding, and given that plant-pesticides are by their very nature toxic substances, all plant-pesticides produced via rDNA methodologies should undergo some form of review under both FIFRA and FFDCA. . . (Ref. 5).

3. *Current status*. In companion documents published elsewhere today in this issue of the **Federal Register**, EPA exempts plant-incorporated protectants derived through conventional breeding from sexually compatible plants. In that document, EPA describes conventional breeding as the creation of progeny through either: The union of gametes, i.e., syngamy, brought together through processes such as pollination, including bridging crosses between plants and wide crosses; or vegetative reproduction. Conventional breeding does not include use of the techniques of genetic engineering. It does not include use of: Recombinant DNA; other techniques wherein the genetic material is extracted from an organism and introduced into the genome of the recipient plant through, for example, micro-injection, macro-injection, micro-encapsulation; or cell fusion.

In this supplemental document, EPA specifically requests comment on two proposed alternative regulatory approaches for plant-incorporated protectants derived through genetic engineering (e.g., rDNA) from plants sexually compatible with the recipient plant.

B. Description of Alternative Proposals

Under the first alternative, all plant-incorporated protectants derived from plants sexually compatible with the recipient plant would be exempt

regardless of the technique used to introduce the plant-incorporated protectant into the plant. Under the second alternative, EPA would establish a notification process that would implement a screening procedure to determine whether a plant-incorporated protectant derived through genetic engineering from a plant sexually compatible with the recipient plant qualified for exemption.

1. *Exemption of all plant-incorporated protectants derived from plants sexually compatible with recipient plant.* EPA will review comment on this supplemental proposal, and reevaluate risk in light of recent information and the comments. If EPA concludes that all plant-incorporated protectants derived from plants sexually compatible with the recipient plant meet the criteria for an exemption from all FIFRA requirements, except for the adverse effects reporting requirement at 40 CFR 174.71, and the requirements of a tolerance under section 408 of the FFDCA for the residues of such plant-incorporated protectants, the following language would be substituted in the regulatory text at 40 CFR part 174.

i. *FIFRA.* The following language would be substituted at 40 CFR 174.25:

§ 174.25 Plant-incorporated protectant from sexually compatible plant.

A plant-incorporated protectant is exempt if all of the following conditions are met:

(a) The genetic material that encodes the pesticidal substance or leads to the production of the pesticidal substance is derived from a plant that is sexually compatible with the recipient plant.

(b) The genetic material that encodes the pesticidal substance or leads to the production of the pesticidal substance has never been derived from a source that is not sexually compatible with the recipient plant.

(c) The active ingredient has not been functionally modified from the source.

Sexually compatible, when referring to plants, would mean capable of forming a viable zygote through the union of two gametes, including the use of bridging crosses or wide crosses between plants. Sexually compatible would include the recombination that occurs in hybridization between sexually compatible plants, e.g., the formation of a viable zygote by the pollination of one corn plant with another. It would also include plant-incorporated protectants that normally occur in the plant, when such plants are propagated vegetatively, e.g., banana.

Functionally modified from the source, when referring to plant-incorporated protectants only, would mean the genetic material that encodes a pesticidal substance or leads to the production of a pesticidal substance, has been modified in such a way that the pesticidal substance produced from the genetic material in the recipient plant is functionally different than the pesticidal substance produced in the source. In the 1994 proposal (59 FR at 60524), EPA explained that in proposing the exemptions the Agency did not intend to exempt plant-incorporated protectants that are significantly different in function from the plant-incorporated protectant as it occurs in the source. EPA believes this limitation would be appropriate because rearrangements or modifications of the genetic sequence encoding a pesticidal substance could, for example, result in a plant-incorporated protectant with significantly different functions from the function in the source plant. For example, if the pesticidal substance is an enzyme, it could be modified so that it acts on a different substrate in the recipient plant than it did in the source plant (Refs. 6 and 7). Such a significantly modified plant-incorporated protectant would not be eligible for the exemption because it would not present risks similar to the substance prior to modification, nor would the base of experience on which EPA relies for support of the exemption necessarily be relevant. If the genetic material encoding the pesticidal substance has been modified in such a way that the pesticidal substance functions differently in the recipient plant than it did in the source plant, the analysis performed to determine that the plant-incorporated protectant poses a low probability of risk to the environment and is not likely to cause unreasonable adverse effects to the environment even in the absence of regulatory oversight under FIFRA, would not apply. EPA does not intend that the concept of functionally modified from the source would apply to modifications, in the sequence of the genetic material portion of the plant-incorporated protectant, that may be needed to achieve correct expression, but which have no significant effect on the specificity or function of the pesticidal substance.

In order to clearly indicate in the regulatory text that significantly modified plant-incorporated protectants would not be covered by this exemption, EPA would include a statement that the exemption does not apply to a plant-incorporated protectant that has been functionally modified from the source, and a definition of functionally modified from the source at § 174.3 as follows:

Functionally modified from the source, when referring to plant-incorporated protectants only, means the genetic material that encodes a pesticidal substance or leads to the production of a pesticidal substance has been modified in such a way that the pesticidal substance produced from the genetic material in the recipient plant is functionally different than the pesticidal substance produced in the source.

The definition of ''bridging crosses between plants'' would continue to read as follows:

Bridging crosses between plants means the utilization of an intermediate plant in a cross to produce a viable zygote between the intermediate plant and a first plant, in order to cross the plant resulting from that zygote with a third plant that would not otherwise be able to produce viable zygotes from the fusion of its gametes with those of the first plant. The result of the bridging cross is the mixing of genetic material of the first and third plant through the formation of an intermediate zygote.

EPA is also considering whether to modify the definition of ''wide cross'' by including ''protoplast fusion.'' In part, this will depend on the comment received in response to this proposal (see Unit III.D.6.), and on whether EPA receives information demonstrating that novel exposures would be unlikely even with such an expanded definition.

''Genetic material that encodes for a pesticidal substance'' or leads to the production of a pesticidal substance does not include regulatory regions or noncoding, nonexpressed nucleiotide sequences.

ii. *FFDCA section 408.* To exempt all residues of the pesticidal substance portion of plant-incorporated protectants derived from plants sexually compatible with the recipient plant, regardless of the method by which the plant-incorporated protectant is introduced into the plant, EPA would substitute the following language at 40 CFR 174.479:

§ 174.479 Pesticidal substance from sexually compatible plant; exemption from the requirement of a tolerance.

Residues of a pesticidal substance that is part of a plant-incorporated protectant derived from a sexually compatible plant are exempt from the requirement of a tolerance if all the following conditions are met:

(a) The genetic material that encodes for the pesticidal substance or leads to the production of the pesticidal substance is derived from a plant that is sexually compatible with the recipient food plant.

(b) The genetic material that encodes for the pesticidal substance or leads to the production of the pesticidal substance has never been derived from a source that is not sexually compatible with the recipient plant.

(c) The active ingredient has not been functionally modified from the source.

(d) The residues of the pesticidal substance are not present in food from the plant at levels that are injurious or deleterious to human health.

2. *Case-by-case review of eligibility for exemption through notification process*. EPA also requests comment on a notification process that would implement a screening procedure for plant-incorporated protectants derived through genetic engineering from plants sexually compatible with the recipient plant.

Under this alternative to registration, as part of the final rule EPA would establish criteria to determine whether a plant-incorporated protectant derived through genetic engineering from plants sexually compatible with the recipient plant is ''substantially equivalent'' to a plant-incorporated protectant that could have been derived through conventional breeding from plants sexually compatible with the recipient plant. Anyone intending to sell or distribute a plant-incorporated protectant could submit a notification to EPA seeking a determination that a plant-incorporated protectant qualified for this exemption, accompanied by an analysis demonstrating that the plant-incorporated protectant derived through genetic engineering from plants sexually compatible with the recipient plant is substantially equivalent to a plant-incorporated protectant derived through conventional breeding from sexually compatible plants. The Agency would review the submission and evaluate it against the regulatory criteria to determine whether the plant-incorporated protectant met the criteria for an exemption. At the end of this process, the submitter would receive a letter describing EPA's conclusion. If EPA determines that the plant-incorporated protectant met the criteria, it would be exempt from further regulation under FIFRA, except for the adverse effects reporting requirement at 40 CFR 174.71. However, if EPA determines that the plant-incorporated protectant is not substantially equivalent to a plant-incorporated protectant derived through conventional breeding from sexually compatible plants, a registration would be required prior to its sale or distribution, as well as, if residues of the plant-incorporated protectant are in or on food or feed, a tolerance exemption.

This proposed alternative would be an intermediate measure between exemption of the plant-incorporated protectant and registration, and would ensure that those plant-incorporated protectants derived through genetic engineering from plants sexually compatible with the recipient plant are as safe as those derived through conventional breeding. It would allow the Agency to conduct a case-by-case review of these products to address those endpoints with which the commenters expressed the greatest concern over the strength of the Agency's factual basis for exempting the group as a whole. This notification procedure would, however, impose a lower degree of oversight than the standard requirements of pesticide registration. For example, such ''substantially equivalent'' plant-incorporated protectants would only be subject to the adverse effects reporting requirements at 40 CFR 174.71; unlike registered pesticides, manufacturers would not be required to obtain establishment numbers or submit section 7 production reports. Moreover, the plant-incorporated protectants would not be required to bear FIFRA labels. Nor would the Agency envision requiring the submission of the standard battery of toxicity testing currently required under 40 CFR part 158; rather, only data relevant to a determination of substantial equivalence would be required to be submitted.

Any person who sells or distributes in commerce a plant-incorporated protectant derived through genetic engineering without having obtained either a determination of equivalence or a registration would violate FIFRA section 12(a)(1)(A). Products sold or distributed in commerce in violation of section 12 are subject to seizure, pursuant to FIFRA section 13. In addition, any person selling or distributing such products are subject to the penalties provided in FIFRA section 14.

This option would only exempt a plant-incorporated protectant from the registration requirements under FIFRA. If the plant-incorporated protectant was intended to be used in a food plant, resulting in pesticide chemical residues, a tolerance exemption would need to be established, prior to the introduction of the food in commerce. Without a tolerance exemption, any food bearing residues of the plant-incorporated protectant would be adulterated, pursuant to section 402(a)(2)(B) of FFDCA, and subject to seizure by FDA. An application for an exemption from the tolerance requirement could be submitted concomitantly with the submission for exemption from FIFRA registration requirements.

i. *Criteria for determining substantial equivalence*. Currently, EPA believes that the following considerations could be developed into criteria relevant to determining whether a plant-incorporated protectant is substantially equivalent to a plant-incorporated protectant that could have been derived through conventional breeding from sexually compatible plants.

a. The source of the gene of interest is a plant sexually compatible with the recipient plant, and the active ingredient has not been functionally modified from the source.

b. Any pesticidal substance is not present at deleterious or injurious levels.

c. The plant-incorporated protectant has the same tissue expression pattern, including levels of expression, observed in varieties of the recipient plant currently in widespread agricultural use or consumed by the U.S. population.

d. Any inert ingredient is on the list of approved inert ingredients at subpart X of 40 CFR part 174.

Prior to adopting criteria in any final rule, EPA would seek the advice of its SAP on criteria appropriate for evaluating whether a plant-incorporated protectant derived through genetic engineering from plants sexually compatible with the recipient plant is substantially equivalent to a plant-incorporated protectant that could have been derived through conventional breeding from sexually compatible plants.

ii. *Where to submit notification*. By mail, written notifications would be submitted to: Document Processing Desk (7504C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460. In person, deliver requests to: Environmental Protection Agency, Crystal Mall #2, Room 258, Document Processing Desk, 1921 Jefferson Davis Hwy., Arlington, VA. In order to expedite processing, the request must be marked ''Attention: Plant-Incorporated Protectant Notification Review.''

iii. *Contents of notification*. The notification could include, for example:

a. Name and address of requester and name, address, e-mail address, and telephone number of a person who may be contacted for further information.

b. Data or information relating to a determination that the specific plant-incorporated protectant and any inert ingredient(s) are substantially equivalent to a plant-incorporated protectant derived through conventional breeding from sexually compatible plants. Such information could include:

- A detailed description of the introduced genetic material, including certification that the organism(s) that is the source of the genetic material encoding the pesticidal substance is a plant that is sexually compatible with the recipient plant.
- The source of any selectable markers.
- The product(s) of the genetic material, and whether and how the

products (both active and inert ingredients) are expected to affect the behavior of the recipient plant.

• Information on all regulatory sequences including those affecting specificity of tissue expression and information on the level of expression of the structural genes.

• Stability of the introduced genetic material.

c. Any other information the requester might consider relevant.

iv. *CBI.* To assert a claim of confidentiality, the requester would have to comply with the applicable procedures in 40 CFR 174.9. Section 174.9(a) states that failure to assert a claim of confidentiality at the time the information is submitted to EPA will be considered a waiver of confidentiality for the information submitted, and the information may be made available to the public, subject to section 10(g) of FIFRA, with no further notice to the submitter.

v. *EPA review.* EPA would review and evaluate notifications as expeditiously as possible. If the request received by EPA is complete (e.g., no additional information is required by EPA or submitted by the requester as supplemental information, or no amendment to the request made), EPA would complete its evaluation in between 150 and 180 days of receipt of the request. EPA may require additional information from the submitter in order to assess the equivalence of the plant-incorporated protectant derived through genetic engineering to a plant-incorporated protectant derived through conventional breeding from sexually compatible plants. Should EPA require additional information or the requestor submit supplemental information, more than 150 to 180 days may be required to complete the assessment. At the conclusion of the review, EPA will supply a letter to the submitter describing the Agency's evaluation and determination.

The submitter may supplement, amend, or withdraw his or her notification in writing, without EPA approval, at any time prior to EPA's determination. The withdrawal of a request shall be without prejudice to the resubmission of the notification at a later date.

C. Request for Comment on Proposed Alternative Regulatory Approaches

EPA requests comment on the following issues for the proposed alternatives described in Unit III.B. EPA requests that respondents comment on the proposed alternative proposals, and include consideration of the issues described in Unit III.D. in their comments on Unit III.C.

1. *Distinction between proposed approaches.* The two proposed regulatory alternatives distinguish between plant-incorporated protectants on the basis of the process by which the plant-incorporated protectant has been introduced into the plant. EPA requests comment on whether a distinction based on the process of genetic modification is justified in light of the state of the science, including the specific questions and risk concerns raised by the comments received in response to the Agency's 1994 proposal, and briefly described in Unit III.D.

Given the issues described in Unit III.D. with respect to plant-incorporated protectants derived through genetic engineering from plants sexually compatible with the recipient plant, are such products sufficiently analogous to plant-incorporated protectants derived from conventional breeding that the Agency can rely on the factual basis, described in companion documents published elsewhere in this issue of the **Federal Register** for plant-incorporated protectants derived through conventional breeding, to support the exemption in the proposed regulatory alternative described in Unit III.B.1.

2. *Notification process.* EPA requests comment on the utility of a notification process for determining whether a plant-incorporated protectant derived through genetic engineering from plants sexually compatible with the recipient plant is equivalent to a plant-incorporated protectant derived through conventional breeding from sexually compatible plants. EPA is particularly interested in comments addressing whether this level of regulatory oversight is necessary to address the potential risks from plant-incorporated protectants derived through genetic engineering from plants sexually compatible with the recipient plant, and whether this level of oversight would adequately address the safety questions surrounding these products. Can the factual basis, described in companion documents published elsewhere in this issue of the **Federal Register** for plant-incorporated protectants derived through conventional breeding, be used on a case-by-case basis to support exemption in the proposed regulatory alternative described in Unit III.B.2.

EPA requests comment on the criteria described in Unit III.B.2.i. for evaluating ''substantial equivalence.'' For example, EPA requests comment on whether reliance on plants currently in widespread agricultural use, or consumed by the U.S. population is an appropriate standard, or whether it would be more appropriate to compare the resulting plant-incorporated protectant to its parental organisms. The Agency would welcome any information or data that might be of assistance in developing proposed criteria for use in its potential notification process. EPA would particularly welcome comment on whether the criteria described in Unit III.B.2.i., would capture all of the potential pleiotropic effects of concern with respect to this subgroup of plant-incorporated protectants. In light of the fact that FDA is proposing to review all genetically engineered foods for possible effects resulting from the point of insertion, EPA requests comment on whether there is any need for EPA to also examine this endpoint. The Agency is concerned that the final criteria not prevent it from examining all possible parameters of interest, but also recognizes the need for determinate criteria for this option to function effectively.

EPA requests comment on whether the potential information needs described in Unit III.B.2.iii. are adequate for demonstrating substantial equivalence with plant-incorporated protectants derived through conventional breeding from sexually compatible plants. EPA solicits comment on whether there are any additional types of information that might be useful for demonstrating substantial equivalence.

3. *Variant of notification process for broader group of plant-incorporated protectants.* Some components in plants are widely distributed across the plant kingdom and thus may be found in many plant populations, some of which are not sexually compatible with each other. EPA requests comment on whether a notification process similar to one described in Unit III.B.2. could be developed for plant-incorporated protectants from outside the gene pool of the recipient plant, but nonetheless equivalent to those that evolved within the gene pool of the recipient plant.

EPA notes that to develop a notification process for such plant-incorporated protectants, EPA must first develop criteria to describe such plant-incorporated protectants. EPA would seek the advice of its SAP in developing proposed criteria. Some of the factors EPA might ask the SAP to consider in developing criteria for proteinaceous substances include amino acid sequence homology, post-translational processing, structure, stability, receptor/ligand specificity, substrate specificity and equivalence of reaction products. For non-proteinaceous plant-incorporated protectants, the chemical composition

and structure of the introduced plant-incorporated protectant could be compared with the plant-incorporated protectants that are normally components of the recipient plant. This information on composition and structure could then be related to the function of the introduced plant-incorporated protectant. Other factors that might also be considered in this determination include:

i. When during the plant's life cycle the pesticidal substance is produced.

ii. In which part of the plant (e.g., leaves, roots, fruit) the pesticidal substance is produced.

iii. The levels at which it is produced. EPA would welcome any information or data that might be of assistance in developing proposed criteria for use in this variant of a potential notification process.

D. Request for Comment on Risk Issues

Several risk issues have been raised for plant-incorporated protectants derived through genetic engineering from plants sexually compatible with the recipient plant. EPA requests comment on these issues, described in this unit, in the context of the two proposed alternative regulatory approaches described in Unit III.B.

1. *Levels of toxicants*? Some comments described toxic substances naturally occurring in plants in sexually compatible populations, and expressed concern that EPA's 1994 proposal to exempt all plant-incorporated protectants derived from sexually compatible plants did not include consideration of the potential for risk associated with increases in levels of such substances. These comments implied that such increases are more likely to occur with plant-incorporated protectants derived through genetic engineering from sexually compatible plants. One commenter stated, for example, that use of ''artificial regulators (regardless of source) may allow genes to escape natural dampening mechanisms and to be produced at extremely high levels not found in naturally occurring or traditionally bred plants. Artificial promotors may also result in toxins being produced in tissues where they are not ordinarily produced, or in some cases in every cell of the plant'' (Ref. 8). Another commenter stated that ''EPA appears to be ignoring a basic axiom of toxicology, e.g., the dose makes the poison'' (Ref. 5).

In a companion document published elsewhere in this issue of the **Federal Register**, EPA, recognizing that increases in levels of toxicants can occur in conventional breeding as well as in varieties developed through genetic engineering, imposed a condition on the exemption at 40 CFR 174.479 to address this concern. In order to allow EPA and FDA to act expeditiously, should a rare instance of levels high enough to render food injurious or deleterious occur, residues of the pesticidal substances derived through conventional breeding from sexually compatible plants qualify for exemption from the tolerance requirement only if the ''residues of the pesticidal substance are not present in food from the plant at levels that are injurious or deleterious to human health.''

EPA requests comment on whether, in the context of food and FFDCA section 408 requirements, such a limitation is sufficient to address the same concern for residues of pesticidal substances derived through genetic engineering from plants sexually compatible with the recipient plant, should EPA exempt this later subgroup, as described in Unit III.B.1.

EPA also requests comment on whether, in the context of FIFRA requirements, this condition would be sufficient to address the concerns that have been raised with respect to potential effects on nontarget organisms for plant-incorporated protectants derived through genetic engineering from plants sexually compatible with the recipient plant.

EPA requests comment on whether such a limitation is meaningful for those plant-incorporated protectants not in plants used for food or feed (e.g., trees), given that deleterious or injurious substances in such semi-managed plants naturally tend to greater ranges of expression than seen in crop plants, including higher ranges of expression (Ref. 9).

Commenters also discussed the potential for changes in promotors or other regulatory elements to affect tissue specific expression of toxicants, i.e., where previously a toxicant was expressed only in trace amounts in the edible part of the plant, a new promotor might result in high levels of expression in the edible part. EPA requests comment on whether such events are more likely to occur with plants-incorporated protectants derived through genetic engineering than with those derived through conventional breeding from sexually compatible plants. EPA also requests comment on whether the condition placed on the tolerance exemption at 40 CFR 174.479, that the ''residues of the pesticidal substance are not present in food from the plant at levels that are injurious or deleterious to human health'' are adequate to address this concern for plant-incorporated protectants derived through genetic engineering from plants sexually compatible with the recipient plant in the context of FFDCA section 408. Is this condition sufficient to address the concern for FIFRA?

2. *Potential for production of a novel toxicant*? In developing the final rule published elsewhere in this issue of the **Federal Register** in companion documents, EPA also considered the possibility that expression of a transgenic protein could result in the plant producing a toxicant not observed in either of the parent species. An example of this would be the case of somatic hybrids between *Solanum brevidans* and *S. tuberosum* producing the toxicant, demissine, not found in either parental line. *Laurila et al.* (Ref. 10) advanced the hypothesis that the hydrogenase enzyme of *S. brevidans* produced the toxicant by hydrogenating solanine, a compound that is found in *S. tuberosum* but not in *S. brevidans*. Portions of the metabolic pathways necessary to produce this substance apparently existed in the parental species, and the mingling of the genetic material resulted in a complete pathway for production of demissine. This example suggests that novel metabolic pathways could be created in a plant through the introduction of a single gene, should other components of the pathway already be present in the plant. EPA requests comment on whether there is any difference in the probability of this occurring in plants in sexually compatible populations into which the plant-incorporated protectant was introduced by genetic engineering as compared to conventional breeding.

3. *Consequences of transfer of ability to produce higher levels of a plant-incorporated protectant to wild or weedy relatives?* EPA also received comments on the potential for a food crop or other commercial plant engineered to produce unusually high levels of a plant-incorporated protectants to ''interbreed with a wild, weedy relative which in turn would become very resistant to certain insect pests. The wild relative, now free from certain pest damage, could increase in number and either become a much worse pest itself or disrupt an ecosystem. . .'' (Ref. 5). Gene flow from crop plants to wild relatives has been observed in plants developed through conventional breeding in sexually compatible populations (Refs. 11 and 12). It has not yet been established whether gene flow into feral populations, from either genetic engineered or conventionally bred plants, can endow wild relative

populations with a selective advantage that might enhance their potential for weediness.

Given that wild relatives of crop plants are likely to already possess traits similar to those in related crop plants, and express these traits at a higher range of levels than crop plants, what is the probability that outcrossing of the ability to express such traits at high levels from crop plants to wild or weedy relatives, would give the wild relatives a competitive advantage?

EPA also requests comment on whether this phenomenon could result in significantly different consequences when comparing gene flow between plant-incorporated protectants derived through genetic engineering from sexually compatible plants as compared to plant-incorporated protectants derived through conventional breeding from sexually compatible plants.

4. *Does use of antibiotic or herbicide resistance or other selectable markers present risk?* Because genetic engineering techniques are so precise, a gene can be excised from the source organism without unwanted, extraneous genetic material. The precise gene can then be introduced into the recipient organism. However, there can be other genetic information on the construct used to introduce the desired gene, and although this genetic information may also be precise, it may not be part of the gene pool of the recipient plant, e.g., genes for herbicide resistance used as a selectable marker. In a companion document published elsewhere in this issue of the **Federal Register**, EPA describes its determination that the Agency will adopt the definition of inert ingredient it proposed in 1994. An inert ingredient for plant-incorporated protectants is ''any substance, such as a selectable marker, other than the active ingredient, where the substance is used to confirm or ensure the presence of the active ingredient, and includes the genetic material necessary for the production of the substance, provided that genetic material is intentionally introduced into a living plant in addition to the active ingredient.'' In that same companion document, EPA also describes the qualification that a plant-incorporated protectant can only be exempt if the inert ingredient(s) used with an exempt active ingredient is on the list of approved inert ingredients at subpart X of 40 CFR part 174.

EPA anticipates that a plant-incorporated protectant qualifying for exemption under the proposed regulatory alternative described in Unit III.B.1. would be composed of an active ingredient derived through genetic engineering from a plant sexually compatible with the recipient plant and an ingredient on the approved list at subpart X of 40 CFR part 174. In light of this assumption, and given that the inserted structural gene of interest (for EPA's purposes, the gene encoding the pesticidal substance) is taken from the same gene pool in which it normally exists, EPA requests comment on whether, even if the structural gene of interest in the inert ingredient is derived from a source not sexually compatible with the recipient plant, the plant-incorporated protectant can still be considered to be ''substantially equivalent'' to a plant-incorporated protectant that could have been derived through conventional breeding. Specifically, EPA requests comment on whether the risks associated with such plant-incorporated protectants derived through genetic engineering are any greater that the risks associated with plant-incorporated protectants derived through conventional breeding.

5. *Should protoplast fusion be included in the definition of wide cross?* EPA requests comment on whether protoplast fusion should be added to the definition of wide crosses. In the official comment period for the November 23, 1994 **Federal Register**, EPA received one comment that suggested protoplast fusion should be included among the techniques listed in the definition of wide crosses between plants. A protoplast is made in the laboratory through the removal of the cell walls of somatic cells. A somatic cell is a type of cell that forms plant vegetative tissues and organs and is distinguished from a germ cell which undergoes meiosis to produce reproductive tissues (e.g., pollen and egg cells). In the technique of protoplast fusion, protoplasts from two different plants are fused together, producing a hybrid somatic cell with a genetic makeup resulting from the combination and sorting of the two plant genomes. The hybrid somatic cell is grown on specialized media into a mature plant. In support of the request, the commenter argued that the hybridization of somatic cells (i.e., protoplast fusion) has a history of use to artificially induce sexual compatibility. For the most part, the more closely related the plants donating the protoplasts used for the fusion, the more likely a viable hybrid will be obtained. Currently, in a companion document published elsewhere in this issue of the **Federal Register**, EPA specifically excludes cell fusion from the definition of conventional breeding, with cell fusion defined as ''the fusion *in vitro* of two or more cells or protoplasts.''

EPA requests comment on whether protoplast (or cell) fusion, or alternatively, some subgroup of fusions (e.g., intraspecific or intrageneric), should be included in the definition of wide crosses in light of the following dietary and environmental considerations. First, in the example provided in Unit III.D.2. describing the potential for creation of new toxicants, dimissine arose through the fusion of protoplasts of *S. tuberosum* and *S. brevidans*. Second, the FDA in its 1992 ''Statement of Policy: Foods Derived from New Plant Varieties'' (57 FR 22984, May 29, 1992) expresses a concern that protoplast fusion might confer on food from the host plant the allergenic properties of food from the donor plant.

IV. Notice of Data Availability and Request for Comment

In April 2000, the NAS released a report entitled ''Genetically Modified Pest-Protected Plants: Science and Regulation'' (Ref. 13). Prepared by an expert committee, this report examined the proposals offered by EPA in the November 23, 1994, **Federal Register** (59 FR 60496). This report recommended that EPA reconsider the Agency's proposed exemptions, raising a number of questions, primarily with respect the Agency's factual support for the exemptions. EPA requests comment on the information, analyses, and conclusions contained in the NAS report only with respect to those portions of its original proposals that remain pending. EPA is not soliciting comments on any issues beyond those raised specifically by the information contained in the NAS report; for example, the NAS report raised no issues with respect to the Agency's analyses of the human health risks associated with viral coat proteins. Any comments submitted on such issues will be treated as having been submitted after the close of the comment period, as the Agency has twice solicited comment on these issues, in 1994 and 1997.

The NAS report presents a number of competing considerations without necessarily providing the Agency with a ready basis for resolving these issues. For example, the report (Ref. 13 at 44-46) states:

> The 1987 NAS report noted that the risks associated with rDNA-engineered organisms are ''the same in kind'' as those associated with unmodified organisms and organisms modified by other methods. The committee agrees with that statement for pest-protected plants in that both transgenic and conventional plants may pose certain risks and the resulting plant phenotypes are often similar. Transgenic breeding techniques can be used to obtain the same resistance

phenotype as conventional methods (for example resistance to microbial pathogens, nematodes, and insects). Because both methods have the potential to produce organisms of high or low risk, the committee agrees that the properties of a genetically modified organism should be the focus of risk assessments, not the process by which it was produced (point 3).

In this regard, the committee found that:

There is no strict dichotomy between or new categories of the health and environmental risks that might be posed by transgenic and conventional pest-protected plants.

The committee recognizes that the magnitude of the risk varies on a product by product basis. The committee also agrees with points 1 and 2 in the sense that the potential hazards and risks associated with the organisms produced by conventional and transgenic methods fall into the same general categories. As this report discusses, toxicity, allergenicity, effects of gene flow, development of resistant pests, and effects on non-target species are concerns for both conventional and transgenic pest-protected plants.

The committee agrees with the 1987 NAS principles in that the magnitude of quantitative risk does not depend on the genetic-modification process. It depends on the new genes that are expressed in the plant. End points of risk (such as illness in humans and declines in nontarget species) can be the same regardless of whether a specific new gene was transferred by conventional or transgenic methods. For example, if the same alkaloid gene is transferred by sexual hybridization or *Agrobacterium*-mediated insertion, the risk should be similar. If a gene coding for a novel trait is transferred by transgenic methods, but cannot be transferred by conventional methods, it is the expressed trait that requires scrutiny, not the method of transfer.

Yet by contrast, on page 128, the report states:

The committee recognizes the realistic limitations of overseeing the pesticidal substances in conventional pest-protected plants and, given their history of safe use, recognizes that there are practical reasons for exempting those substances. However, the committee questions the scientific basis used by EPA for this exemption because no strict dichotomy or new categories appear to exist between the risks to health and the environment that might be posed by conventional and transgenic pest-protected plant products (section 2.2.1).

The categorical exemption also applies to transgenic pest-protected plant products that contain transgenes from sexually compatible species, and the committee questions the scientific basis for this exemption as well, specifically because the genes and gene products can be expressed at concentrations far greater than the concentrations at which they are naturally expressed (sections 2.4.1 and 2.5.2). Even though the risks of many transgenic pest-protected plants containing genes from sexually compatible species are expected to be low and would justify exemption, lack of experience with these products and public concern over genetic engineering suggest that a blanket exemption for them is inadvisable.

EPA requests comment on how to best reconcile these competing considerations.

V. Proposed Alternative Regulatory Approaches to Plant-Incorporated Protectants Based on Viral Coat Proteins

This Unit solicits additional comment on the two alternative regulatory approaches the Agency discussed in greater detail in the 1994 proposal (59 FR 60496, e.g., see 60525 through 60528). EPA solicits additional public comment on these alternatives in light of the issues raised by the NAS report, as well as on the issues raised by commenters on the 1994 proposal. The Agency intends to consider public comments and make final determinations to complete these other rulemakings within 9 to 12 months after the close of the comment period for the supplemental proposal, which is currently set at 30 days. Until the Agency takes a final action on these other exemptions, the Agency intends to maintain its current practices on regulation of plant-incorporated protectants.

A. History

Coat proteins are those substances that viruses produce to encapsulate and protect the nucleic acids comprising their genetic material. When the genetic material encoding the information for making the coat protein of a plant virus is introduced into a plant's genome, the plant becomes resistant to infection by the virus donating the genetic material for the coat protein (and frequently to viruses closely related to the donor virus) (Refs. 14 and 15). This resistance is termed viral coat protein mediated-resistance or vcp-mediated resistance (Refs. 14 and 15). Coat proteins from plant viruses intended to be produced and used in living plants for vcp-mediated resistance to viral disease, along with the genetic material necessary to produce the coat proteins, are plant-incorporated protectants.

1. *1994 Proposal.* In the 1994 proposal, EPA proposed to exempt from all FIFRA requirements, except for the adverse effects reporting requirement at § 174.71, all plant-incorporated protectants based on coat proteins from plant viruses (Option 1) (59 FR at 60525). EPA also described an alternative option (Option 2) offering a more limited exemption (59 FR 60526). Under this alternative option, the exemption would be limited to those plant-incorporated protectants based on coat proteins from plant viruses that would have the least potential to confer selective advantage on free-living wild plant relatives of the plants containing these plant-incorporated protectants. Under Option 2, a coat protein would be exempt if:

The pesticidal substance is a coat protein from a plant virus and the genetic material necessary to produce the coat protein has been introduced into a plant's genome, and the plant has at least one of the following characteristics:

(1) The plant has no wild relatives in the United States with which it can successfully exchange genetic material, i.e., corn, tomato, potato, soybean, or any other plant species that EPA has determined has no sexually compatible wild relatives in the United States.

(2) It has been demonstrated to EPA that the plant is incapable of successful genetic exchange with any existing wild relatives (e.g., through male sterility, self-pollination).

(3) If the plant can successfully exchange genetic material with wild relatives, it has been empirically demonstrated to EPA that existing wild relatives are resistant or tolerant to the virus from which the coat protein is derived or that no selective pressure is exerted by the virus in natural populations.

2. *Public comments.* In response to its November 23, 1994 **Federal Register** request for comment on the proposal to exempt plant-incorporated protectants based on the coat proteins of plant viruses, EPA received 65 comments. Many of the comments supported Option 1. Some of the comments supported adoption of Option 2. In the opinion of these commenters, Option 2 appropriately addresses concerns about the potential effects of outcrossing of plant-incorporated protectants based on coat proteins from plant viruses from crop plants to wild or weedy relatives. These comments pointed out that there is scientific evidence indicating that crops may transfer traits to wild relatives, and that many crops grown in the United States have wild relatives that are either native or have been introduced. These comments questioned the adequacy of available data to evaluate the probability that outcrossing of plant-incorporated protectants based on coat proteins from plant viruses could confer a selective advantage on wild or weedy relatives of crop plants. Approximately one-third of the comments opposed the exemption of plant-incorporated protectants based on coat proteins from plant viruses. Most of these comments offered no explanation for their opposition. Those who explained their opposition cited among their concerns, a potential for creation of more aggressive weeds and disturbance to centers of diversity

3. *Current status*. The Agency received scientific information both from commenters supporting Option 1 and commenters supporting Option 2. In this supplemental document, EPA requests additional public comment on the proposed alternative approaches discussed in the 1994 **Federal Register** and the risk considerations associated with weediness raised in comment. EPA will consider all comments received on this proposal, including comments received in response to the original proposal in 1994, and any comments received in response to this supplemental document, in arriving at a decision on how to proceed.

B. Description of Proposed Modification to Language of Proposed Exemption

Were EPA to implement either of the two options proposed in 1994, it would modify the language to clearly state that plant-incorporated protectants that are significantly different in structure or function from the plant-incorporated protectant as it occurs in the source would not be exempt.

In the 1994 proposal (59 FR at 60524), EPA explained that the Agency did not intend to exempt plant-incorporated protectants that are significantly different in structure or function from the plant-incorporated protectant as it occurs in the source. EPA believes this limitation is appropriate for coat proteins from plant viruses because rearrangements or modifications of the genetic sequence encoding a pesticidal substance could, for example, result in a plant-incorporated protectant with significantly different functions from the function in the source plant. For example, if the pesticidal substance is an enzyme, it could be modified so that it acts on a different substrate in the recipient plant than it did in the source plant (Refs. 6 and 7). Such a significantly modified plant-incorporated protectant would not be eligible for the exemption. It would not necessarily present risks similar to the substance prior to modification, nor would the base of experience on which EPA relies for support of the exemption necessarily be relevant.

Should EPA implement either Option 1 or Option 2, the Agency would include a statement that the exemption does not apply to a plant-incorporated protectant functionally modified from the source.

C. Request for Comment

The NAS report recommends that the:

> EPA should not categorically exempt viral coat proteins from regulation under FIFRA. Rather, EPA should adopt an approach, such as the Agency's alternative proposal. . ., that allows the agency to consider the gene transfer risks associated with the introduction of viral coat proteins to plants. (Ref. 13 at 132)

The NAS bases its recommendation primarily on a lack of information on the effects of the transfer of genes conferring pest resistance from crop plants to weedy or wild relatives.

EPA solicits any additional information that might assist the Agency in determining whether it should implement Option 1, i.e., exempt all plant-incorporated protectants based on viral coat proteins, or Option 2, i.e., an approach that allows the Agency to evaluate the gene transfer risks associated with the introduction of viral coat proteins to each candidate plant. In addition, in light of the fact that USDA reviews potential plant-pest related issues relative to viral coat proteins, EPA requests comment on whether there is any need for EPA to also examine this endpoint.

EPA solicits comment on whether outcrossing of plant-incorporated protectants based on coat proteins from plant viruses could confer a selective advantage on wild or weedy relatives of crop plants, and if so, which crop plants. EPA would be particularly interested in receiving data on this issue.

EPA specifically requests comment on whether acquired virus-resistance could, for example: (1) Allow a wild plant to increase its range or population density; and/or (2) permit a plant's population density to increase so that the plant dominates a community where it was far less common before acquisition of the trait.

As a condition of the exemption, EPA could require applicants for the exemption to submit studies or generate data on the gene transfer risks associated with the candidate plant-incorporated protectant. Alternatively, EPA could require some degree of monitoring beyond that which would be required by the adverse effects reporting requirement. EPA requests comment on whether either of these approaches is necessary to address the concerns raised by the NAS and the commenters, or whether sufficient data currently exists to evaluate the gene transfer risks presented by the class of products that would be covered under either Option 1 or 2.

VI. Proposal on Plant-Incorporated Protectants that Act Primarily by Affecting the Plant

In this Unit, EPA solicits additional public comment on this proposed exemption and on the scientific issues raised by the NAS report (Ref. 13) and in comments received on the 1994 proposal. The Agency intends to consider public comments and make final determinations to complete these other rulemakings within 9 to 12 months after the close of the comment period for the supplemental proposal, which is currently set at 30 days. Until the Agency takes a final action on these other exemptions, the Agency intends to maintain its current practices on regulation of plant-incorporated protectants.

A. History

In the 1994 proposal (59 FR at 60525), EPA stated that one of the Agency's primary goals in regulating pesticides is to control the potential for adverse effects of pesticides on nontarget organisms. EPA reasoned that an important component in the evaluation of this potential is the way in which the pesticidal substance acts on the target pest since it would also likely affect nontarget organisms through the same mechanism. EPA further reasoned that some plant-incorporated protectants could act through mechanisms that are less likely to be directly toxic. The Agency stated a belief that although it is possible for these substances to adversely affect nontarget organisms, in most cases, they would pose significantly lower levels of environmental risk than plant-incorporated protectants with a generalized toxic mechanism of action. EPA identified those plant-incorporated protectants it thought would act in this manner as those that act primarily by affecting the plant so that the pest is inhibited from attaching to the plant, penetrating the plant's surface, or invading the plant's tissue.

1. *1994 Proposal*. In the November 23, 1994 **Federal Register**, EPA proposed to exempt from all FIFRA requirements, except for the adverse effects reporting requirement at 40 CFR 174.71, plant-incorporated protectants that act primarily by affecting the plant. The proposed regulatory text presented criteria to define mechanisms of action that exert the pesticidal action primarily by affecting the plant. The proposed language reads as follows:

> The pesticidal substance acts primarily by affecting the plant so that the target pest is inhibited from attaching to the plant, penetrating the plant, or invading the plant's tissue in at least one of the following ways:
>
> (i) The pesticidal substance acts as a barrier to attachment of the pest to the host plant, a structural barrier to penetration of the pest into the host plant, or a structural barrier to spread of the pest in the host plant, for example, through the production of wax or lignin, or length of trichomes (plant hairs).

(ii) The pesticidal substance acts in the host plant to inactivate or resist toxins or other disease-causing substances produced by the target pest.

(iii) The pesticidal substance acts by creating a deficiency of a plant nutrient or chemical component essential for pest growth on/in the host plant.

In the 1994 **Federal Register** document, EPA also indicated that it was considering extending this exemption to include substances such as plant hormones, because plant hormones act within the plant to ''primarily affect the plant'' and do not act directly on a target pest (59 FR at 60525, 60531). EPA requested public comment on whether plant hormones should be included in the exemption for plant-incorporated protectants that act primarily by affecting the plant.

2. *Public comments*. EPA received 23 comments that addressed this proposed exemption. A majority of comments supported the exemption of plant-incorporated protectants that act primarily by affecting the plant. The comments opposing the exemption primarily expressed concern about the potential for outcrossing of the trait from crop plants to wild relatives to increase weediness in the wild relatives. These concerns were variously described as concerns that outcrossing of these plant-incorporated protectants to wild relatives might result in the following outcomes: First, produce hardier plants that become weeds in agro-ecosystems; second, produce hardier plants that displace less hardy types; or, third, adversely impact nontarget organisms that depend for their survival on interactions with wild plants. Some comments urged EPA, in order to address the concerns, to adopt an approach that would subject a plant-incorporated protectant to regulation based on whether the plant-incorporated protectant was introduced into the recipient plant through use of rDNA or other techniques of modern biotechnology.

Fourteen comments responded to EPA's request for comment on whether to exempt plant hormones because they act primarily by affecting the plant. Most comments favored the exemption of plant hormones, stating that plant hormones act within the plant to affect the plant's behavior and do not have a toxic mode of action. A few comments favored exemption of plant hormones except when there is clear indication of unreasonable adverse effects to the plants as can occur in some plant diseases mediated by microorganisms. The comments disagreeing with the exemption expressed concern that outcrossing of plant hormones from crop plants to wild relatives might confer competitive advantage on the wild relatives.

3. *Current status*. In this supplemental document, EPA requests additional public comment on this proposed exemption and several risk issues raised in comment. EPA will consider all comments received on this proposal in arriving at a determination, including comments received in response to the original proposal in 1994, and any comments in response to this supplemental document.

B. Proposed Modification to Language of Proposed Exemption

The Agency is considering whether to modify the language of the proposed exemption as follows:

1. *Hypersensitive response*. Some comments suggested the hypersensitive response in plants would fall within the definition of a plant-incorporated protectant that functions by primarily affecting the plant. EPA understands the hypersensitive response to involve compounds that initiate, potentiate, or enhance hypersensitive or hypersensitive-type responses that result in area-specific necrosis in response to microbial invasion of plant tissue, thus limiting spread of the pathogen within the plant. EPA believes that the criteria of this exemption as proposed in 1994 would include substances involved in the hypersensitive response. EPA requests comment on whether, for regulatory clarity, the Agency should add language to the regulatory text at 40 CFR part 174 to clearly show that substances involved in hypersensitive or hypersensitive-type responses are exempt. That language would read as follows:

(iv) By initiating, potentiating, or enhancing hypersensitive or hypersensitive-type responses that, in response to invasion by a phytopathogen, results in necrosis of specific areas of plant tissue thereby limiting the spread of the pathogen in or on the plant.

2. *Functionally modified from the source*. As described in Unit V.B., in proposing the exemptions the Agency did not intend to exempt plant-incorporated protectants that are significantly different in structure or function from the plant-incorporated protectant as it occurs in the source (59 FR at 60524). The discussion at Unit III.B.i. and Unit V.B., applies equally to this proposed exemption for plant-incorporated protectants that act primarily by affecting the plant. In order to clearly indicate in the regulatory text that significantly modified plant-incorporated protectants would not be covered by this exemption, EPA would include a statement in this exemption that it does not apply to a plant-incorporated protectant that has been functionally modified from the source.

To this end, the following language would be added to the proposed exemption:

A plant-incorporated protectant acts primarily by affecting the plant if the plant-incorporated protectant has not been functionally modified from the source and the pesticidal substance:

(1) . . . .

The proposed definition of ''functionally modified from the source'' as described at Unit III.B.i., would also apply to this proposed language.

3. *Plant hormones*. Plant hormones are substances produced by plants that play a major role in the regulation of plant growth by either accelerating or retarding, through physiological action, the rate of growth or rate of maturation of the plant, or the produce thereof (Ref. 16). Known classes of plant hormones occurring naturally in plants are auxins, cytokinins, ethylene, abscisic acid, and gibberellins. Plant hormones are active in the living plant in very small quantities.

Were EPA to add specific language to this proposed exemption indicating that plant hormones act primarily by affecting the plant, the Agency would also add a definition of plant hormone in the context of plant-incorporated protectants at § 174.3 as follows:

Plant hormone, when referring to plant-incorporated protectants only, would mean naturally occurring auxins, cytokinins, ethylene, abscisic acid, and gibberellins, produced and used in a living plant, or in the produce thereof.

C. Request for Comment

1. *Hypersensitive response*. EPA solicits comment on whether the substances involved in the hypersensitive response meet the proposed criteria and act primarily by affecting the plant. EPA requests comment on whether the language it proposes in this supplemental document adequately describes substances involved in the hypersensitive response.

2. *Functionally modified from the source*. EPA solicits comment on whether the language it has proposed adequately addresses its concern that the genetic material not be functionally modified from the source. EPA solicits comment on whether this language effectively ensures that the genetic material may not be so modified that it has a significantly different specificity or function in the recipient plant than it did in the source plant, yet permits modifications that may be needed to

achieve correct expression, but which have no significant effect on the specificity or function of the pesticidal substance.

3. *Plant hormones*. EPA solicits comment on whether the proposed definition of plant hormone appropriately describes this group of plant substances, and whether these substances act primarily by affecting the plant.

EPA solicits comment on whether plant hormones present a low probability of risk, particularly in light of the NAS report statement that plant hormones ''often cause multiple changes in plants, including changes in secondary metabolites that might be toxic'' (Ref. 13 at 133).

EPA also specifically solicits comment on the NAS statement that ''there is a need to consider separately the impact of plant hormones on nontarget species and the potential for the genes that code for these substances to move to feral populations of weedy relatives of the crop, where they could increase recipient plants' fitness'' (Ref. 13 at 133). In light of this NAS statement, EPA specifically solicits information supporting the broad exemption that EPA proposed in 1994 for plant-incorporated protectants that act by primarily affecting the plant. EPA also requests comment on whether there are subgroups within this category of plant-incorporated protectants for which information exists supporting a finding that the products present a low probability of risk. Commenters are encouraged to submit such information to the Agency.

EPA also solicits comment on the comment received in response to the 1994 proposal that favored exemption of plant hormones except when there is clear indication of unreasonable adverse effects to the plants as can occur in some plant diseases mediated by microorganisms (Ref. 17, for example). The Agency cannot determine the direct relevance that these pathogenic effects would have to this specific exemption, and requests additional information.

4. *Are there subgroups of this category meeting the FFDCA section 408(c) exemption standard*? A plant-incorporated protectant in or on food cannot be exempted from FIFRA requirements unless an exemption from the FFDCA section 408 requirement of a tolerance has been issued for the residues of the plant-incorporated protectant in or on food. If a plant-incorporated protectant is not used in a crop used as food (e.g., the plant-incorporated protectant is produced and used in an ornamental plant), the FFDCA section 408 requirements do not need to be considered when determining whether the plant-incorporated protectant can be exempted from FIFRA requirements. However, if a plant-incorporated protectant is used in a crop used as food (e.g., the plant-incorporated protectant is produced and used in corn), the FFDCA section 408 requirements must be considered when determining whether the plant-incorporated protectant can be exempted from FIFRA requirements. To be considered for full exemption from FIFRA requirements, exemptions from the FFDCA requirement of a tolerance must exist for all of the residues. (See Unit VII.D.1.iv. of the companion document published elsewhere in this issue of the **Federal Register** on regulations for plant-incorporated protectants under FIFRA for additional details).

When EPA proposed in 1994 to exempt from FIFRA requirements plant-incorporated protectants that act primarily by affecting the plant, it did not, because of the broad range and variety of plant-incorporated protectants comprising this category, propose a companion proposal exempting residues of the substance portion of plant-incorporated protectants in this category from the FFDCA section 408 requirement of a tolerance. The Agency would also be interested in comments that describe subgroups of plant-incorporated protectants in this category that would meet the FFDCA section 408(c) standard for an exemption. EPA will treat such comments as a petition for a tolerance exemption pursuant to FFDCA section 408(d); commenters therefore are encouraged to review sections 408(b)(2), (c) and (d) in preparing their comments.

VII. Documents in the Official Record

As indicated in Unit I.B.2., the official record for this supplemental proposal has been established under docket control number OPP–300370B, the public version of which is available for inspection as specified in Unit I.B.2.

A. References

The following books, articles, and reports were used in preparing this supplemental proposal and were cited in this document by the number indicated:

1. USDA/APHIS. 1987. Plant pests; Introduction of genetically engineered organisms or products; Final rule. (52 FR 22891, June 16, 1987).

2. USDA/APHIS. 1993. Genetically engineered organisms and products; Notification procedures for the introduction of certain regulated articles; and petition for nonregulated status; Final rule. (58 FR 17044, March 31, 1993).

3. USDA/APHIS. 1997. Genetically engineered organisms and products; Simplification of requirements and procedures for genetically engineered organisms. (62 FR 23945, May 2, 1997).

4. EPA. Joint meeting of the EPA Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP), Subpanel on Plant-pesticides and the EPA Biotechnology Science Advisory Committee (BSAC), Subcommittee on Plant-Pesticides. January 21, 1994. Final report.

5. Hansen, M. and J. Halloran. In a letter dated February 22, 1995 on docket numbers OPP–300367 through 300371.

6. International Food Biotechnology Council. 1990. Biotechnologies and food; Assuring the safety of foods produced by genetic modification. *Regulatory Toxicology and Pharmacology*. Vol. 12. Academic Press. New York, New York.

7. Wilks, H. M., A. Cortes, D. C. Emery, D. J. Halsall, A. R. Clarke, and J. J. Holbrook. 1992. Opportunities and limits in creating new enzymes. *Enzyme Engineering XI*. Edited by D.S. Clark and D. A. Estell. Annals of the New York Academy of Sciences. Vol. 672. The New York Academy of Sciences. New York, New York.

8. Rissler, J. and M. Mellon. In a letter dated January 23, 1995, on docket control numbers OPP–300367 through OPP–300371.

9. EPA issue paper. 1994. FIFRA: Benefit and environmental risk considerations for inherent plant-pesticides.

10. Laurila, J., I. Lasko, J. P. T. Valkonen, R. Hiltunen, and E. Pehu. 1996. Formation of parental type and novel glycoalkaloids in somatic hybrids between Solanum brevidans and S. tuberosum. *Plant Science*. 118:145–155.

11. Linder, C. R. Long-Term Introgression of Crop Genes into Wild Sunflower Populations. *Theoretical Applied Genetics*. 87:339–347. 1998.

12. Goldburg, R. In a letter dated February 6, 1995, on docket control number OPP–300370.

13. National Research Council. 2000. Genetically Modified Pest-Protected Plants: Science and Regulation. (Prepublication copy). National Academy Press. Washington DC.

14. Cook, R. J. and C. O. Qualset. 1996. (Eds) Appropriate oversight for plants with inherited traits for resistance to pests. Institute of Food Technologists. http://www.Info&ift.org.

15. EPA. 2000. Economic analysis of the plant-incorporated protectant regulations under the Federal

Insecticide, Fungicide, and Rodenticide Act.

16. EPA. 2000. Summary of public comments and EPA response on issues associated with plant-incorporated protectants for dockets listed in OPP–300368, OPP–300368A, OPP–300369, OPP–300369A, OPP–300370, OPP–300370A, OPP–300371, and OPP–300371A.

B. Additional Information

The following additional sources of information are included in the complete official record for this rulemaking:

The docket identified by the docket control number OPP–300370 for the document entitled ''Proposed Policy: Plant-Pesticides Subject to the Federal Insecticide, Fungicide, and Rodenticide Act and the Federal Food, Drug, and Cosmetic Act'' (59 FR 60496) (FRL–4755–2).

The docket identified by the docket control number OPP–300369 for the document entitled ''Plant-Pesticides Subject to the Federal Insecticide, Fungicide and Rodenticide Act; Proposed Rule'' (59 FR 60519 November 23, 1994) (FRL–4755–3).

The docket identified by the docket control number OPP–300368 for the document entitled ''Plant-Pesticides; Proposed Exemption From the Requirement of a Tolerance Under the Federal Food, Drug, and Cosmetic Act'' (59 FR 60535 November 23, 1994) (FRL–4758–8).

The docket identified by the docket control number OPP–300371 for the document entitled ''Plant-Pesticides; Proposed Exemption From the Requirement of a Tolerance Under the Federal Food, Drug, and Cosmetic Act for Nucleic Acids Produced in Plants'' (59 FR 60542, November 23, 1994) (FRL–4755–5).

The docket identified by the docket control number OPP–300370A for the document entitled ''Plant-Pesticide Subject to the Federal Insecticide, Fungicide, and Rodenticide Act and the Federal Food, Drug, and Cosmetic Act; Reopening of Comment Period'' (61 FR 37891, July 22, 1996) (FRL–5387–4).

The docket identified by the docket control number OPP–300368A for the document entitled ''Plant-Pesticides; Supplemental Notice of Proposed Rulemaking'' (62 FR 27132, May 16, 1997) (FRL–5717–2).

The docket identified by the docket control number OPP–300371A for the document entitled ''Plant-Pesticides; Nucleic Acids; Supplemental Notice of Proposed Rulemaking'' (62 FR 27142, May 16, 1997) (FRL–5716–7).

The docket identified by the docket control number OPP–30069A for the document entitled ''Plant-Pesticides, Supplemental Notice of Availability of Information'' (64 FR 19958, April 23, 1999) (FRL–6077–6).

The docket identified by the docket control number OPP–300368B for the companion document entitled ''Exemption From the Requirement of a Tolerance Under the Federal Food, Drug, and Cosmetic Act for Residues Derived From Sexually Compatible Plants of Plant-Incorporated Protectants (Formerly Plant–Pesticides)'' (FRL–6057–6) published elsewhere in this issue of the **Federal Register**.

The docket identified by the docket control number OPP–300371B for the companion document entitled ''Exemption From the Requirement of a Tolerance Under the Federal Food, Drug, and Cosmetic Act for Residues of Nucleic Acids that are Part of Plant-Incorporated Protectants (Formerly Plant-Pesticides)'' (FRL–6057–5) published elsewhere in this issue of the **Federal Register**.

The docket identified by the docket control number OPP–300369B for the document entitled ''Regulations Under the Federal Insecticide, Fungicide, and Rodenticide Act for Plant-Incorporated Protectants (Formerly Plant-Pesticides)'' (FRL–6057–7) published elsewhere in this issue of the **Federal Register**.

The docket identified by the docket control number OPP–300370B for this document (FRL–6760–4).

Also included in the complete official record for this document are:

1. Public comments submitted in response to the proposals and supplemental documents cited in the Unit III.B. In addition, comments received subsequent to the close of the comment period for the 1994 proposal have been included in the record for this supplemental proposal. This includes a report entitled ''Appropriate Oversight for Plants with Inherited Traits for Resistance to Pests'' (Ref. 14), as well as the NAS report (Ref. 13).

2. Reports of all meetings of the Biotechnology Science Advisory Committee and the FIFRA Science Advisory Panel pertaining to the development of the final rule for plant-incorporated protectants published in companion documents elsewhere in this issue of the **Federal Register**.

3. The Economic Analysis of the final rule for plant-incorporated protectants published in companion documents elsewhere in this issue of the **Federal Register** (Ref. 15) and supporting documents.

4. Support documents and reports.

5. Records of all communications between EPA personnel and persons outside EPA pertaining to this supplemental proposal. (This does not include any inter- and intra-agency memoranda, unless specifically noted in the Indices of the dockets).

6. Published literature that is cited in this document.

7. The response to comments documents pertaining to actions taken by the Agency on dockets OPP–300368, OPP–300368A, OPP–300369, OPP–300369A, OPP–300370, OPP–300370A, OPP–300371, and OPP–300371A (Ref. 16).

VIII. Regulatory Assessment Requirements

This action merely announces the availability of and requests comments on additional data and/or information related to a proposed rule that previously published in the **Federal Register** of November 23, 1994 (59 FR 60519). As such, the regulatory assessment requirements imposed on rulemakings do not apply to this supplemental proposal. Nevertheless, since there have been several revisions to the regulatory assessment mandates that are imposed on rulemakings, the Agency welcomes your comments on the following determinations.

Should the Agency finalize an exemption under FFDCA section 408, and not impose any other requirements, such an action would not require any special considerations under Executive Order 12898, entitled *Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations* (59 FR 7629, February 16, 1994), nor would it involve any technical standards that would require Agency consideration of voluntary consensus standards pursuant to section 12(d) of the National Technology Transfer and Advancement Act of 1995 (NTTAA), Public Law 104–113, section 12(d) (15 U.S.C. 272 note).

Such an action would only directly affect growers, food processors, food handlers and food retailers, not States. It would not impose any enforceable duty or contain any unfunded mandate, and would not otherwise significantly or uniquely affect small governments as described under Title II of the Unfunded Mandates Reform Act of 1995 (UMRA) (Public Law 104–4). It would not require any prior consultation as specified by Executive Order 13084, entitled *Consultation and Coordination with Indian Tribal Governments* (63 FR 27655, May 19, 1998). Executive Order 13175, entitled *Consultation and Coordination with Indian Tribal Governments* (65 FR 67249, November

6, 2000), which took effect on January 6, 2001, revokes Executive Order 13084 as of that date. EPA developed this rulemaking, however, during the period when Executive Order 13084 was in effect; thus, EPA addressed tribal considerations under Executive Order 13084. EPA does not expect its analysis to change, and will fully comply with the requirements of Executive Order 13175 before promulgating any final rules. For the same reasons, EPA does not expect these proposed actions to have any substantial direct effect on States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government, as specified in Executive Order 13132, entitled *Federalism* (64 FR 43255, August 10, 1999). Such an action would not alter the relationships or distribution of power and responsibilities established by Congress in the preemption provisions of FFDCA section 408(n)(4).

Such an action would not require a regulatory flexibility analysis under the Regulatory Flexibility Act (RFA) (5 U.S.C. 601 *et seq.*), because an exemption from the requirement of a tolerance under FFDCA section 408 would not adversely affect any small entities.

This rule is not subject to Executive Order 13211, entitled *Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use* (66 FR 28355, May 22, 2001), because this action is not expected to affect energy supply, distribution, or use.

For information about the applicability of the regulatory assessment requirements to the previously published proposed rule, please refer to the discussion in Unit XI. of that document (59 FR at 60533).

List of Subjects in 40 CFR Part 174

Environmental protection, Agricultural commodities, Pesticides and pests, Plants.

Dated: July 12, 2001.

Christine T. Whitman,

Administrator.

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