ENVIRONMENTAL PROTECTION AGENCY

40 CFR Parts 152 and 174

[OPP–300369B; FRL–6057–7]

RIN 2070–AC02

Regulations Under the Federal Insecticide, Fungicide, and Rodenticide Act for Plant-Incorporated Protectants (Formerly Plant-Pesticides)

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: The substances plants produce for protection against pests, and the genetic material necessary to produce these substances, are pesticides under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), if humans intend to use these substances for ''preventing, repelling or mitigating any pest.'' In this rule, EPA finalizes certain of the proposed rules published in 1994, 1996, and 1997. Specifically, EPA changes the name of this type of pesticide from ''plant-pesticide'' to ''plant-incorporated protectant''; clarifies the relationship between plants and plant-incorporated protectants under FIFRA; exempts from FIFRA requirements plant-incorporated protectants derived through conventional breeding from sexually compatible plants; and establishes a new part in the Code of Federal Regulations (CFR) specifically for plant-incorporated protectants. Procedures are also set forth for Confidential Business Information (CBI); any claim of confidentiality must be substantiated when the claim is made. This rule will benefit the public by ensuring that public health and the environment are adequately protected while reducing burden on the regulated community, thereby potentially reducing costs for consumers.

DATES: This rule is effective September 17, 2001.

FOR FURTHER INFORMATION CONTACT: Philip Hutton, Biopesticides and Pollution Prevention Division, Office of Pesticide Programs (7511C), 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 table is not intended to be exhaustive, but rather provides a guide for readers regarding the types of entities potentially affected by this action. Other types of entities not listed in the table could also be affected. The North American Industrial Classification System (NAICS) codes have been 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 any questions regarding 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/. To access information about EPA's program for biopesticides go directly to the Home Page for the Office of Pesticide Programs at http://www.epa.gov/pesticides/biopesticides.

2. *In person.* The Agency has established an official record for this action under the docket control number OPP–300369B. 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, which includes printed, paper versions of any electronic comments submitted during an applicable comment period, is available for inspection in the Public Information and Record Integrity Branch (PIRIB), Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Highway, 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.

II. Under What Authority Is EPA Issuing The Rule?

A. FIFRA

This rule is promulgated under the authority of FIFRA section 3 and section 25(a) and (b) (7 U.S.C. 136a and 136w(a) and (b)) and FFDCA section 346a and 371.

FIFRA section 3(a) provides, with some exceptions, that no person may distribute or sell in the United States any pesticide that is not registered

under the Act (7 U.S.C. 136a(a)). FIFRA section 2(u) 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)).

Although FIFRA requires the registration of most pesticides, it also authorizes the regulation of unregistered pesticides. FIFRA section 3(a) provides that, to the extent necessary to prevent unreasonable adverse effects on the environment, the Administrator may limit the distribution, sale, or use of any pesticide that is not registered under section 3 of FIFRA, or subject to an experimental use permit under section 5 of FIFRA, or subject to an emergency exemption under section 18 of FIFRA (7 U.S.C. 136a(a)). Pesticides that are ''not registered'' include pesticides that are exempt from FIFRA requirements under section 25(b).

Before EPA may register a pesticide under FIFRA, the applicant must show that the pesticide ''when used in accordance with widespread and commonly recognized practice, . . . will not generally cause unreasonable adverse effects on the environment'' (7 U.S.C. 136a(c)(5)). The term ''environment'' includes ''water, air, land, and all plants and man and other animals living therein, and the interrelationships which exist among these'' (7 U.S.C. 136(j)). FIFRA section 2(bb) defines the term ''unreasonable adverse effects on the environment'' to mean: ''(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 a 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)).

When EPA published its proposed rules and policy for plant-incorporated protectants in 1994, the FIFRA definition of ''unreasonable adverse effects'' contained only the first criterion of unreasonable risk to man or the environment. Subsequently, Congress enacted the Food Quality Protection Act (FQPA) in 1996, and expanded the FIFRA definition of ''unreasonable adverse effects on the environment'' by adding the second criterion of consistency with the standard under section 408 of the Federal Food, Drug, and Cosmetic Act (FFDCA) (Public Law 104–170 (August 3, 1996)). As a result of this change, a pesticide must meet both criteria of the unreasonable adverse effects test to qualify for registration. In the case of a pesticide whose use would not result in residues in or on food, the second criterion would not apply. Once a pesticide has been registered, it may be sold and distributed in the United States.

Section 25(b)(2) of FIFRA allows EPA to exempt, by regulation, any pesticide from some or all of the requirements of FIFRA, if the pesticide is of a character which is unnecessary to be subject to FIFRA in order to carry out the purposes of that Act (7 U.S.C. 136w(b)(2)). EPA interprets FIFRA section 25(b)(2) to authorize EPA to exempt a pesticide or category of pesticides that EPA determines poses a low probability of risk to the environment, and that is not likely to cause unreasonable adverse effects to the environment even in the absence of regulatory oversight under FIFRA.

To determine whether a pesticide qualifies for an exemption under section 25(b)(2), EPA evaluates both the potential risks and benefits of the use of the pesticide. In evaluating a pesticide under the first exemption criterion, whether use of the pesticide poses a low probability of risk to the environment, EPA considers the extent of the potential risks caused by use of the pesticide to the environment, including humans and other animals, plants, water, air and land. Potential risks to humans include dietary risks as well as non-dietary risks such as those resulting from occupational or residential exposure to the pesticide. EPA uses the FFDCA section 408 standard in evaluating dietary risks as discussed in Unit II.B. EPA will not exempt pesticides under section 25(b)(2) that fail the low probability of risk criterion.

In evaluating a pesticide under the second exemption criterion, whether the use of the pesticide is likely to cause unreasonable adverse effects on the environment even in the absence of regulatory oversight under FIFRA, EPA balances all the potential risks to human health, including any dietary risks (see Unit II.B. for a discussion of the relationship between this finding and section 408 of the FFDCA), and risks to the remainder of the environment from use of the pesticide against the potential benefits associated with its use. In balancing risks and benefits, EPA considers the economic, social, and environmental costs and benefits of the use of the pesticide. If the pesticide meets both exemption criteria, EPA may exempt the pesticide from regulation under FIFRA section 25(b)(2).

B. Relationship of FIFRA Exemptions to the FFDCA Section 408 Standard

Under FFDCA section 408(a), a pesticide chemical residue in or on food is not safe unless EPA has issued either: A tolerance for the residue and the residue is within the tolerance limits, or an exemption from the requirement of a tolerance for the residue (21 U.S.C. 346a(a)(1)). FFDCA section 408 authorizes EPA to determine a residue is safe and exempt from the requirement of a tolerance if the Administrator ''. . . has determined that there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information'' (21 U.S.C. 346a(c)(2)(A)). Section 408 of the FFDCA also directs EPA to specifically consider harm that may result to infants and children as a result of pesticide chemical residues. For additional discussion of this standard, see the exemptions from the FFDCA requirement of a tolerance published elsewhere in this issue of the **Federal Register** (i.e., exemptions for residues of plant-incorporated protectants derived through conventional breeding from a plant sexually compatible with the recipient plant, and residues of nucleic acids that are part of a plant-incorporated protectant).

EPA uses the FFDCA section 408 safety standard in evaluating whether a pesticide used in food meets the two FIFRA exemption criteria with respect to human dietary risk. A pesticide in food qualifies under the first FIFRA exemption criterion of low probability of human dietary risk if it meets the FFDCA section 408 standard for an exemption from the requirement of a tolerance. Such a pesticide also meets the second FIFRA exemption criterion of no likely unreasonable adverse effects, with respect to human dietary risks only, if the risks resulting from use of that pesticide are consistent with the FFDCA section 408 exemption standard, and the potential benefits of use outweigh any human health risk even in the absence of regulatory oversight.

A determination that a pesticide chemical meets the safety standard of section 408(c) of the FFDCA may also be relevant to whether a pesticide qualifies for a FIFRA section 25(b)(2) exemption with respect to human health risks arising from other routes of exposure. In

determining whether a pesticide chemical residue is safe, EPA must consider ''available information regarding the aggregate exposure levels of consumers . . . to the pesticide chemical residue and to other related substances, including dietary exposure under the tolerance and all other tolerances in effect for the pesticide chemical residue, and exposures from other non-occupational sources.'' (21 U.S.C. section 346a(b)(2)(D)(vi)). Consequently, a finding that a pesticide qualifies for a tolerance exemption could also demonstrate that the pesticide chemical meets the first exemption criterion of low probability of risk with respect to human health risks arising from other non-occupational routes of exposure. Such a pesticide also meets the second FIFRA exemption criterion of no likely unreasonable adverse effects, with respect to human health risks arising from all non-occupational exposures, if the risks resulting from use of that pesticide are consistent with the FFDCA section 408 exemption standard, and the potential benefits of use outweigh any human health risk even in the absence of regulatory oversight.

However, FIFRA does not provide for exemption of a pesticide in food based solely upon consistency with the FFDCA section 408 exemption standard. At a minimum, EPA also must evaluate risks arising from occupational exposure to humans and determine that such risks meet both exemption criteria. In addition, EPA must evaluate the risks to the environment from the pesticide and determine both that the pesticide poses only a low probability of environmental risks, and that use of the pesticide is not likely to cause any unreasonable adverse effects on the remainder of the environment in the absence of regulation under FIFRA.

III. What is the Background for this Rule?

This final rule establishes certain basic parameters of EPA's regulatory program under FIFRA for plant-incorporated protectants. In this rule, EPA defines the scope of products subject to FIFRA jurisdiction, and identifies the category of products over which it will exert regulatory oversight. EPA also establishes certain fundamental definitions to clarify what will be subject to regulation as a plant-incorporated protectant. The rule also finalizes certain regulatory procedures specific to plant-incorporated protectants. This document also provides some guidance on the way in which the Agency intends to interpret the existing regulations for these products until it is able to establish additional regulations specific to plant-incorporated protectants.

Specifically, the rule clarifies that plants used as biological control agents remain exempt from FIFRA requirements, but that plant-incorporated protectants are not. Second, the rule exempts plant-incorporated protectants derived through conventional breeding from sexually compatible plants. Third, this final rule establishes a new 40 CFR part 174, specifically for plant-incorporated protectants; any additional regulations specific to plant-incorporated protectants will be codified in 40 CFR part 174. The final rule also imposes a requirement at § 174.71, that any person producing an otherwise exempt plant-incorporated protectant for sale and distribution, who obtains any information regarding adverse effects of this otherwise exempt plant-incorporated protectant on human health or the environment report that information to EPA. Finally, the rule includes a provision that any claim of confidentiality must be made at the time of submission and substantiated at the time the claim is made.

A. What Is a Plant-Incorporated Protectant?

Plants have evolved, and thus naturally possess, various mechanisms to resist pests. The mechanisms of resistance can be varied, including, for example, structural characteristics of the plant, the production of 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. Humans have for approximately 10,000 years selected and bred certain plants as sources of, for example, food, feed, and fiber, and a frequently selected characteristic was the ability to resist pests. More recently, humans have developed scientific techniques by which traits from any living organism, including an ability to resist pests, can be introduced into a plant. When humans intend to use substances involved in these mechanisms in plants for ''preventing, destroying, repelling or mitigating any pest,'' the substances are pesticides under the FIFRA definition of pesticide, regardless of whether the pesticidal capability evolved in the plants or was introduced by breeding or through the techniques of modern biotechnology.

The genetic material necessary for the production of such a pesticidal substance also meets the FIFRA statutory definition of a pesticide. Such genetic material is introduced into a plant with the intent of ultimately producing a pesticidal effect even though the genetic material may not, itself, directly affect pests. The pesticidal substance, along with the genetic material necessary to produce it, produced and used in living plants, is designated a ''plant-incorporated protectant'' by EPA.

Plant-incorporated protectants are primarily distinguished from other types of pesticides because they are intended to be produced and used in the living plant. This difference in use pattern dictates in some instances differences in approach. For example, because the plant-incorporated protectant is produced by the plant itself and used in the living plant, exposure considerations in risk assessments may be different, although as noted in Unit VII.D.2., the risk assessment framework used for other types of pesticides can be used for plant-incorporated protectants.

B. Does the Rule Have Any Relevance to Other Types of Pesticides?

Nonviable plant tissues, organs, or parts that are used as pesticides, will not be subject to the provisions of this rule, which will be codified in regulations at 40 CFR part 174. Rather, such pesticides are subject to the regulations found in 40 CFR parts 150 through 173 and 40 CFR parts 177 through 180. An example of this type of pesticide would be the powder, produced by drying and grinding cayenne peppers, dusted on plants to protect them from pests.

Substances that are isolated from a plant's tissues and then applied to plants for pest control will not be subject to the regulations in 40 CFR part 174. Rather these types of pesticides in formulations such as those for foliar application are subject to regulations found in 40 CFR parts 150 through 173 and 40 CFR parts 177 through 180. An example of this type of pesticide would be pyrethrum isolated from chrysanthemum plants, formulated with other ingredients for foliar application, and sprayed on other plants for pest control.

Substances that are synthesized will not be subject to the regulations in 40 CFR part 174. Such pesticides are subject to regulations found in 40 CFR parts 150 through 173 and 40 CFR parts 177 through 180. An example of this type of pesticide is the herbicide, atrazine.

C. What is the History of this Rule?

This rule is an additional step in fully implementing the ''Coordinated Framework for Regulation of

Biotechnology'' of the United States of America which was published in the **Federal Register** by the Office of Science and Technology Policy (OSTP) on June 26, 1986 (51 FR 23302).

EPA sponsored, or cosponsored with other Federal agencies, three conferences dealing with plant related issues: On October 19–21, 1987, a meeting on ''Genetically Engineered Plants: Regulatory Considerations'' at Cornell University, Ithaca, New York; on September 8–9, 1988, a ''Transgenic Plant Conference'' in Annapolis, Maryland; on November 6–7, 1990, a conference on ''Pesticidal Transgenic Plants: Product Development, Risk Assessment, and Data Needs'' in Annapolis, Maryland. Information from these conferences has been incorporated as appropriate in development of this rule.

In developing its approach to plant-incorporated protectants, EPA requested advice from two scientific advisory groups at three meetings. On December 18, 1992, a Subpanel of the FIFRA Scientific Advisory Panel (SAP) was convened to review a draft proposed policy statement and to answer a series of scientific questions concerned primarily with EPA's proposed exemptions under FIFRA. On July 13, 1993, a Subcommittee of the EPA Biotechnology Science Advisory Committee (BSAC) was convened to address a series of scientific questions concerned primarily with EPA's proposed exemptions under the FFDCA. On January 21, 1994, a joint meeting of the Subpanel of the SAP and the BSAC Subcommittee was convened to address a series of scientific questions on approaches to plant-pesticides under both FIFRA and FFDCA. Advice from these scientific advisory groups was considered in finalizing this rule.

EPA published in the November 23, 1994, **Federal Register** a package of five separate documents (59 FR 60496, 60519, 60535, 60542 and 60545) (FRL–4755–2, FRL–4755–3, FRL–4755–4, and FRL–4755–8) which described EPA's policy and proposals for plant-pesticides (now called plant-incorporated protectants) under FIFRA and FFDCA. On July 22, 1996, EPA published a supplemental document in the **Federal Register** (61 FR 37891) (FRL–5387–4) on one aspect of its November 23, 1994, **Federal Register** documents; i.e., how the concept of inert ingredient related to plant-pesticides.

In August of 1996, Congress enacted the FQPA which amended FFDCA and FIFRA. On May 16, 1997, EPA published in the **Federal Register** supplemental documents (62 FR 27132, 27142, 27149) (FRL–5716–6, FRL–5716–7, FRL–5717–2) to provide the public with an opportunity to comment on EPA's analysis of how certain FQPA amendments to FFDCA and FIFRA apply to the proposed exemptions from the FFDCA requirement of a tolerance for two categories of residues relevant to this final rule.

On April 23, 1999, EPA published a supplemental document in the **Federal Register** (64 FR 19958) (FRL–6077–6) soliciting comment on whether to change the name of this type of pesticide.

The documents and reports of the meetings described in this unit are available in the official record for this rule as described in Unit VIII.

D. Other Federal Agencies

EPA is the Federal agency primarily responsible for the regulation ofpesticides. 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 forensuring 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.

IV. What Are the Key Features of the Proposed Rule?

The development of this rule consists of a proposed rule that appeared in the November 23, 1994, **Federal Register** and four supplemental documents affecting the final form of the rule (59 FR 60496, 60519, 60535, 60542, and 60545); a supplemental document that appeared in the July 22, 1996, **Federal Register** (61 FR 37891), two supplemental documents that appeared in the May 16, 1997, **Federal Register** (62 FR 27132, 27142), and a supplemental document that appeared in the April 23, 1999, **Federal Register** (64 FR 19958).

A. What Are the Key Features of the November 23, 1994, **Federal Register***?*

In the November 23, 1994, **Federal Register** document (59 FR 60519), EPA proposed to: first, clarify how the exemption at 40 CFR 152.20 relates to plants used as biological control agents and to plant-incorporated protectants; second, exempt under FIFRA section 25(b)(2), plant-incorporated protectants that are derived from plants closely related to the recipient plant, except for a requirement that sellers or distributors of an otherwise exempt plant-incorporated protectant submit to EPA any information they may obtain regarding potential unreasonable adverse effects caused by an exempt plant-incorporated protectant; and third, establish new part 40 CFR part 174 specifically for plant-incorporated protectants. This document also contained a proposed rule on substantiation of any claim of confidentiality at the time the claim was made.

1. *Clarification of exemption at 40 CFR 152.20; status of plants used as biological control agents with regard to FIFRA requirements.* In the November 23, 1994, **Federal Register** document, EPA proposed to amend 40 CFR 152.20 to clarify that plants used as biological control agents are exempt from FIFRA requirements under section 25(b)(1). The proposed amendment at 40 CFR 152.20 would also indicate that this exemption does not apply to plant-incorporated protectants and would refer the reader to 40 CFR part 174 for regulations, including a listing of exemptions, on plant-incorporated protectants.

2. *Proposed exemption of plant-incorporated protectants derived from plants closely related to the recipient plant.* In 1994, EPA described three options for defining when a plant-incorporated protectant would be exempt because it is derived from plants closely related to the recipient plant. EPA proposed to exempt plant-incorporated protectants derived from plants closely related to the recipient plant based on the rationale that the probability of new exposures from this group of plant-incorporated protectants is very low. Option 1, the Agency's preferred option, used sexual compatibility, including hybridization achieved by wide and bridging crosses, as a measure of relatedness between plants. Under this option, plant-incorporated protectants would be exempt from all FIFRA requirements, except for the 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. Recipient plant was described as the plant into which the plant-incorporated protectant is introduced and in which the plant-incorporated protectant is produced. 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.

Option 2 would utilize the rank of genus as the taxonomic standard for describing closely related plants such that plant-incorporated protectants derived from plants classified in the same genus as the recipient plant would be exempt from all FIFRA requirements, except for the adverse effects reporting requirement. Taxonomy is a system of orderly classification of organisms according to their presumed natural relationships. Taxonomy reflects current scientific observations about phenotypic, and to a certain extent, genotypic, similarities between organisms.

Option 3, also an alternative option, would utilize both the taxonomic rank of genus and sexual compatibility to describe closely related plants. This option would exempt from all FIFRA requirements, except for the adverse effects reporting requirement, plant-incorporated protectants derived from plants classified in the same genus as the recipient plant, as well as plant-incorporated protectants derived from plants sexually compatible with the recipient plant. Under Options 1 and 3, plant-incorporated protectants derived from plants sexually compatible with the recipient plant would be exempt even if the source and recipient plants are classified in different genera.

None of the options offered by the EPA were intended 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 60524).

i. *Associated definitions.* In 1994, pertinent definitions associated with the proposed exemptions included:

''Bridging crosses between plants'' would be 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.

''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-pollination 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.

In 1994, EPA also presented a definition for plant-pesticide, now termed plant-incorporated protectant, and definitions of active and inert ingredient for plant-pesticides.

''Plant-pesticide'' was defined as a pesticidal substance that is produced in a living plant and the genetic material necessary for the production of the substance, where the substance is intended for use in the living plant.

''Active ingredient,'' when referring to plant-incorporated protectants only, was defined as a pesticidal substance that is produced in a living plant and the genetic material necessary for the production of the substance, where the substance is intended for use in the living plant.

''Genetic material necessary for the production'' was defined as: Genetic material that encodes for a pesticidal substance or leads to the production of a pesticidal substance and regulatory regions. It does not include noncoding, nonexpressed nucleotide sequences.

''Inert ingredient,'' when referring to plant-incorporated protectants only, was defined as any substance, such as a selectable marker, other than the active ingredient, and the genetic material necessary for the production of the substance, that is intentionally introduced into a living plant along with the active ingredient, where the substance is used to confirm or ensure the presence of the active ingredient.

''Living plant'' was defined as a plant that is alive, including periods of dormancy, and all viable plant parts/organs involved in the plant's life cycle.

''Noncoding, nonexpressed nucleotide sequences'' were defined as the nucleotide sequences that are not transcribed and are not involved in gene expression. Examples of noncoding, nonexpressed nucleotide sequences include linkers, adapters, homopolymers, and sequences of restriction enzyme recognition sites.

ii. *Potential exemption criterion based on process.* The Agency also requested

in the 1994 **Federal Register** document (50 FR 60514, 60530), comment on the utility of an exemption criterion based on the process (e.g., rDNA) used to introduce the plant-incorporated protectant into a plant. In this approach, plant-incorporated protectants developed through techniques other than those of modern biotechnology would be exempted, e.g., 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.

iii. *Reporting of unreasonable adverse effects for exempted plant-incorporated protectants*. In 1994, EPA proposed to require, under FIFRA section 3(a), that any person who sells or distributes any otherwise exempt plant-incorporated protectant, who obtains any information regarding potential unreasonable adverse effects on human health or the environment, must within 30 days of receipt of such information submit the information to EPA. This provision was proposed to enable the Agency to address unforeseeable events from use of otherwise exempt plant-incorporated protectants. (This reporting requirement is referred to, in this preamble, as the ''adverse effects reporting requirement.'')

3. *Proposed new 40 CFR part 174*. In the November 23, 1994, **Federal Register** document, EPA proposed to establish a new part in the CFR, 40 CFR part 174, specifically for plant-incorporated protectants. Establishment of a new part would allow the Agency to consolidate regulations specifically applicable to plant-incorporated protectants in one part of the CFR. EPA believed such a consolidation would be appropriate and justified because of the characteristics that distinguish plant-incorporated protectants from other types of pesticides. The proposed consolidation was expected to benefit the public by providing greater focus, enhanced clarity, and ease of use, because all the regulations specific for plant-incorporated protectants would be in one part of title 40. The proposed 40 CFR part 174 would include, for example, definitions that are generally applicable throughout part 174, exemptions from FIFRA regulation, and a subpart for tolerances and exemptions from the requirement of a tolerance published under FFDCA section 408 for residues of plant-incorporated protectants.

4. *Proposed rule regarding upfront substantiation of confidential business information*. EPA proposed in 1994 that any claim of confidentiality would have to be made at the time of submission and substantiated at the time the claim is made.

B. What Issues Were Discussed in the Supplemental Federal Register *Documents?*

Subsequent to publication of the November 23, 1994 **Federal Register** document (59 FR 60519), EPA published four supplemental documents relevant to this document. These supplemental documents are described below.

1. *July 22, 1996*. On July 22, 1996, EPA published a supplemental document in the **Federal Register** (61 FR 37891) on one aspect of its November 23, 1994, **Federal Register** documents; i.e., how the concept of inert ingredient related to plant-incorporated protectants. In 1994, EPA stated that an inert ingredient for plant-incorporated protectants would be ''any substance, such as a selectable marker, other than the active ingredient, and the genetic material necessary for the production of the substance, that is intentionally introduced into a living plant along with the active ingredient, where the substance is used to confirm or ensure the presence of the active ingredient.'' However, additional information caused EPA to request further public comment on its treatment of inert ingredients, including whether there should be inert ingredients for plant-incorporated protectants.

2. *May 16, 1997*. In August of 1996, Congress enacted the FQPA which amended the FFDCA and FIFRA. On May 16, 1997, EPA published in the **Federal Register** two supplemental documents (62 FR 27132, 27142) to provide the public with an opportunity to comment on EPA's analysis of how certain FQPA amendments to FFDCA and FIFRA affect the proposed tolerance exemptions, and thus, to the proposed exemption of certain plant-incorporated protectants from FIFRA requirements. These supplemental documents are discussed in detail in companion documents published elsewhere in this issue of the **Federal Register** addressing tolerance exemptions for pesticide chemical residues derived through conventional breeding from sexually compatible plants and residues of nucleic acids that are part of a plant-incorporated protectant.

3. *April 23, 1999*. In response to the request that EPA consider another name for this type of pesticide, the Agency published in the April 23, 1999 **Federal Register** (64 FR 19958) a document requesting comment on the advisability of substituting an alternative name for the term ''plant-pesticide,'' and requesting appropriate alternative names for this class of pesticides. EPA also specifically requested comment on whether the alternative name, ''plant-expressed protectants,'' would be an acceptable name for this category of pesticides. EPA noted that if the Agency changed the name of the pesticides termed, ''plant-pesticides,'' the change would only affect the name. It would not affect the status of the pesticidal substance or the genetic material necessary to produce it. The Agency also noted that even with a different name, these would still be pesticides under FIFRA section 2(u), and a change of name would not affect any regulatory requirements.

V. What are the Key Features of this Final Rule?

In this final rule, EPA, first, clarifies that plants used as biological control agents remain exempt from FIFRA requirements, as well as clarifying the relationship between plants and plant-incorporated protectants; second, issues an exemption for a category of plant-incorporated protectants; and third, establishes a new 40 CFR part 174, specifically for plant-incorporated protectants. This rule also imposes a requirement at 40 CFR 174.71 that any person producing, for sale and distribution an otherwise exempt plant-incorporated protectant, who obtains any information regarding adverse effects of this otherwise exempt plant-incorporated protectant on human health or the environment, report that information to EPA. Finally, the rule includes a provision that any claim of confidentiality must be made at the time of submission and substantiated at the time the claim is made.

A. Clarification of Exemption at 40 CFR 152.20; Status of Plants Used as Biological Control Agents with Regard to FIFRA Requirements

This final rule amends 40 CFR 152.20 to clarify that plants used as biological control agents remain exempt from FIFRA regulation, but plant-incorporated protectants will be subject to the requirements of FIFRA unless otherwise exempted. The final rule also refers the reader to 40 CFR part 174 for regulations, including a list of exemptions, on plant-incorporated protectants.

B. Exemption of Plant-Incorporated Protectants Derived Through Conventional Breeding from Sexually Compatible Plants

This rule exempts from all FIFRA requirements, except for the adverse effects reporting requirements at 40 CFR

174.71, plant-incorporated protectants that are derived through conventional breeding from sexually compatible plants. The exempt plant-incorporated protectants represent a subcategory of the plant-incorporated protectants described in Option 1 in the November 23, 1994, **Federal Register** document (59 FR 60522). (EPA is seeking additional comment in a supplemental document published elsewhere in this issue of the **Federal Register** on whether all plant-incorporated protectants derived from plants sexually compatible with the recipient plant should be exempt from FIFRA requirements, regardless of how they are introduced into the recipient plant.)

The following language appears in 40 CFR 174.25 to describe this subcategory:

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 from a plant that is sexually compatible with the recipient plant.

(b) The genetic material has never been derived from a source that is not sexually compatible with the recipient plant.

The following language addressing inert ingredients in plants derived through conventional breeding from sexually compatible plants is added to 40 CFR 174.485, subpart X:

An inert ingredient, and residues of the inert ingredient, are exempt if all of the following conditions are met:

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

(b) The genetic material has never been derived from a source that is not sexually compatible with the recipient food plant.

(c) The resides of the inert ingredient are not present in food from the plant at levels that are injurious or deleterious to human health.

1. *Associated definitions*. Pertinent definitions associated with the exemption include:

''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.

''Cell fusion'' means the fusion *in vitro* of two or more cells or protoplasts.

''Conventional breeding of plants'' means 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. It does not include use of any one of the following technologies: 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.

''Genome'' means the sum of the heritable genetic material in the plant, including genetic material in the nucleus and organelles.

''Recombinant DNA'' means the genetic material has been manipulated *in vitro* through the use of restriction endonucleases and/or other enzymes that aid in modifying genetic material, and subsequently introduced into the genome of the plant.

''Sexually compatible,'' when referring to plants, means a viable zygote is formed only through the union of two gametes through conventional breeding.

''Source'' means the donor of the genetic material that encodes a pesticidal substance or leads to the production of a pesticidal substance,

''Vegetative reproduction'' means: In seed plants, reproduction by apomixis; and in other plants, reproduction by vegetative spores, fragmentation, or division of the somatic body.

''Wide crosses'' means 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-pollination and post-pollination hormone treatments, manipulation of chromosome numbers, embryo culture, or ovary and ovule cultures.

Pertinent associated definitions in 40 CFR 174.3, several of which are discussed in Unit VII.B.8., include:

''Active ingredient'' means a pesticidal substance that is intended to be produced and used in a living plant, or in the produce thereof, and the genetic material necessary for the production of such a pesticidal substance.

''Genetic material necessary for the production'' means both: Genetic material that encodes a substance or leads to the production of a substance, and regulatory regions. It does not include noncoding, nonexpressed nucleotide sequences.

''Inert ingredient'' means 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 the genetic material is intentionally introduced into a living plant in addition to the active ingredient.

''Living plant'' means a plant, plant organ, or plant part that is alive, viable or dormant. Examples of plant parts include, but are not limited to, seeds, fruits, leaves, roots, stems, flowers and pollen.

''Noncoding, nonexpressed nucleotide sequences'' means the sequences are not transcribed and are not involved in gene expression. Examples of noncoding, nonexpressed nucleotide sequences include, but are not limited to, linkers, adaptors, homopolymers, and sequences of restriction recognition sites.

''Pesticidal substance'' means a substance that is intended to be produced and used in a living plant, or in the produce thereof, for a pesticidal purpose during any part of a plant's life cycle (e.g., in the embryo, seed, seedling, mature plant).

''Plant-incorporated protectant'' means a pesticidal substance that is intended to be produced and used in a living plant, or in the produce thereof, and the genetic material necessary for the production of such a pesticidal substance. It also contains any inert ingredient contained in the plant, or produce thereof.

''Produce thereof,'' when used with respect to plants containing plant-incorporated protectants only, means a product of a living plant containing a plant-incorporated protectant, where the pesticidal substance is intended to serve a pesticidal purpose after the product has been separated from the living plant. Examples of such products include, but are not limited to, agricultural produce, grains and lumber. Products such as raw agricultural commodities bearing pesticide chemical residues are not ''produce thereof'' when the residues are not intended to serve a pesticidal purpose in the produce.

''Recipient plant'' means the living plant in which the plant-incorporated protectant is intended to be produced and used.

Other definitions, relevant for plant-incorporated protectants only, can be found at 40 CFR 174.3. In this final rule, ''plant'' means an organism classified using the 5-kingdom classification system of Whittaker (Ref. 1) in the kingdom, Plantae. Therefore, the term ''plant'' includes, but is not limited to, bryophytes such as mosses, pteridophytes such as ferns,

gymnosperms such as conifers, and angiosperms such as most major crop plants.

2. *Reporting of adverse effects for exempted plant-incorporated protectants.* This document publishes a requirement under FIFRA section 3(a) that any person who produces, for sale or distribution an otherwise exempt plant-incorporated protectant, who obtains any information regarding adverse effects on human health or the environment alleged to have been caused by the plant-incorporated protectant, must submit such information to EPA. EPA must receive the report within 30 calendar days of receipt of such information. The language of the requirement is set forth at 40 CFR 174.71, subpart D.

C. Establishment of 40 CFR Part 174

This final rule establishes a new 40 CFR part 174, specifically for plant-incorporated protectants. Subpart A sets forth definitions specific for plant-incorporated protectants, including definitions that are generally applicable throughout part 174. Subpart A also contains procedures for confidential business information. Exemptions from FIFRA are contained in subpart B. Subpart D sets forth the unreasonable adverse effects reporting requirement at § 174.71. A subpart W is established for tolerances and exemptions from the requirement of a tolerance published for residues of plant-incorporated protectants under FFDCA section 408. Subpart X lists the inert ingredients that may be used with plant-incorporated protectants that are exempt from FIFRA and FFDCA requirements.

D. Upfront Substantiation of Confidential Business Information

Procedures for confidential business information are set forth at 40 CFR part 174, subpart A. The rule requires that any claim of confidentiality must accompany the information at the time the information is submitted to EPA, and must be substantiated at the time the claim is made.

VI. How Do the Proposed Rule and Final Rule Differ?

This final rule is adopted with several changes from the 1994**Federal Register** proposed rule. As discussed in the supplemental document published in the April 23, 1999 **Federal Register** (64 FR 19958), EPA has changed the name of this type of pesticide from ''plant-pesticide'' to ''plant-incorporated protectant'' for reasons described at Unit VII.B.2. A second significant change is due to the 1996 FQPA amendment to FIFRA. Because of this amendment, and as discussed in supplemental documents published in the May 16, 1997, **Federal Register** (62 FR 27133, 27143, 27150), ''a pesticide used in or on food that does not meet the FFDCA section 408 safety standard also would pose an unreasonable adverse effect under FIFRA and would not qualify for an exemption from the requirements of FIFRA under FIFRA section 25(b)(2).'' EPA revises the language at 40 CFR 174.21 to add the general qualification that a plant-incorporated protectant used in a food plant can be exempt from FIFRA requirements only if residues of the plant-incorporated protectant in or on food or feed qualify for an exemption from the requirement of a tolerance under FFDCA section 408. (See Unit II. and Unit VII.D.1.iv. for additional discussion). EPA has also determined it will adopt the definition of inert ingredient it proposed for plant-incorporated protectants in 1994 and includes language at 40 CFR 174.21, subpart X, to implement this decision.

EPA in this rule finalizes only a portion of the exemptions it proposed in 1994; specifically, the Agency exempts plant-incorporated protectants derived through conventional breeding from plants sexually compatible with the recipient plant. EPA has received comments that raised significant questions on its 1994 proposed rule, and the Agency is currently considering how to address these questions. In a supplemental document published elsewhere in this issue of the **Federal Register** EPA solicits additional public comment on the various options it is considering to respond to the comments it has already received.

EPA has also narrowed the adverse effects reporting requirement at 40 CFR 174.71 so that only persons who produce plant-incorporated protectants for sale and distribution are responsible for submitting information to EPA concerning adverse effects on human health or the environment caused by the otherwise exempt plant-incorporated protectant. EPA narrowed this requirement in response to comments suggesting that the proposed language could lead to the submission of information that was not relevant to EPA's primary concern of adverse effects caused by the plant-incorporated protectant.

Some modifications, primarily for clarity, or clarification, have also been made to the language of the exemption and associated definitions. These modifications are discussed in this document. Discussion of these modifications can also be found in the documents (Ref. 2) summarizing public comments and EPA response on issues associated with plant-incorporated protectants which can be found in the record for this rule as described in Unit VIII.

VII. Discussion of Final Rule and Public Comments

In this unit, EPA discusses the final rule and summarizes comments it received on the November 23, 1994, **Federal Register** documents. EPA reviewed and considered all comments received on the documents published in the November 23, 1994, **Federal Register** and prepared detailed responses to these comments. These can be found at appropriate points in this preamble, and in the Agency's summary of public comments and EPA's response on issues associated with plant-incorporated protectants (Ref. 2), which is located in the official record for the rule as described in Unit VIII.

A. From Whom Did EPA Receive Comment?

In response to the package of documents published in the **Federal Register** in 1994, EPA received letters from industry, academia, professional and trade associations, government agencies, state regulatory authorities, public interest groups, and private citizens. Some of the commenters sent separate letters for each of the five dockets associated with the 1994 **Federal Register** documents. Other commenters sent a single letter addressed to all five dockets.

On July 22, 1996, EPA published in the **Federal Register** (61 FR 37891) a supplemental document seeking additional comment on how it should view the concept of inert ingredient with regard to plant-incorporated protectants. EPA received comments in response to that supplemental document. On May 16, 1997, EPA published in the **Federal Register** (62 FR 27132, 27142, 27149) supplemental documents to provide the public an opportunity to comment on EPA's analysis of how certain amendments to FFDCA and FIFRA by the FQPA apply to EPA's proposed exemptions under FIFRA for plant-incorporated protectants derived from closely related plants, and proposed exemptions under FFDCA for residues of these plant-incorporated protectants and received comment. On April 23, 1999, EPA published in the **Federal Register** (61 FR 19958) a supplemental document on whether to rename this type of pesticide. EPA received comments on that supplemental document. Copies of all comments received are available in the official record for the rule as described in Unit VIII.

EPA also received comments after the comment period for the rule had closed. Eleven scientific societies sent a report entitled ''Appropriate oversight of plants with inherited traits for resistance to pests'' (Ref. 3). The National Academy of Sciences produced a report entitled ''Genetically modified pest-protected plants: Science and regulation'' (Ref. 4). These comments did not raise issues beyond those that had been raised by comments submitted during the comment period for the rule. Therefore, EPA has not included these comments as part of this rulemaking, and will not respond to them in this action.

B. What Are the Major Comments on EPA's Approach?

More comments supported EPA's approach than opposed it. Comments on EPA's approach to plant-incorporated protectants can be categorized as follows. In general, those comments supporting EPA's approach agree that FIFRA gives EPA the authority to regulate substances that plants produce for protection against pests if humans intend to use these substances for preventing, destroying, repelling or mitigating any pest. Second, the commenters believe an approach that regulates the substance while exempting the plant from regulation is appropriate. Some comments, while in general supporting the approach, had reservations about the definition of plant-incorporated protectant, and definitions directly associated with the definition of plant-incorporated protectant. Others, while recognizing EPA's authority under FIFRA, thought an approach to regulation based on whether genetic engineering, e.g., recombinant DNA (rDNA), was used to introduce genetic material for pesticidal purposes into plants, better addressed risk and public concerns. These commenters urged EPA to implement such an approach.

Those comments opposing EPA's approach can in general be described as: First, those opposed to designating plant defense substances as pesticides, including those that believe that FIFRA should only apply to chemical pesticides; second, those who urged a more narrow definition of plant-incorporated protectant; third, those who believe that use of non-governmental peer review and standards of practice accepted in the plant breeding industry are adequate and EPA oversight is unnecessary; and fourth, those who believe that EPA's approach discriminates against rDNA technology and that any discrimination against rDNA technology is unscientific. There also appears to be some confusion evidenced in comments concerning the concept of ''intent'' in the FIFRA section 2 definition of pesticide. Some comments expressed concern that the term, ''pesticide,'' has a negative connotation with the public. Some of these commenters requested that, at a minimum, plant defense substances not be given the name ''plant-pesticide.''

1. *How can plant defense substances be pesticides?* EPA received seven comments that expressed concern with the designation of defense substances produced by plants as pesticides. Most of these comments stated that it was inappropriate to consider plant defense substances to be pesticides and questioned the Agency's determination that plant defense substances are pesticides.

FIFRA section 2(u) defines ''pesticide'' to include any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest. Plant defense substances are clearly pesticides under the FIFRA section 2 definition of pesticide when humans intend to use them ''for preventing, destroying, repelling, or mitigating any pest'' regardless of how the pesticidal capabilities were introduced into the plant (e.g., whether by traditional breeding or through the techniques of modern biotechnology). The suggestion that substances, or mixtures of substances, in plants that humans intentionally use for preventing, destroying, repelling, or mitigating a pest, should not be considered pesticides is not tenable. If the substances were isolated from the plant and sold as pesticides, no one would argue that they were pesticides. Clearly, substances in plants that humans intend to use for preventing, destroying, repelling or mitigating a pest meet the FIFRA section 2 definition of pesticide and Congress has specifically made EPA responsible for regulating pesticides under FIFRA and FFDCA section 408.

2. *Why is EPA giving these pesticides a different name?* EPA recognizes the unique use pattern of these pesticides, which are produced and used in the living plant. Thus, in the November 23, 1994, **Federal Register** (59 FR 60496), EPA suggested giving these types of pesticides a unique name, ''plant-pesticides,'' in order to distinguish them from chemical, microbial, or biochemical pesticides. EPA believes a unique name for this type of pesticides benefits the public by providing the means to more readily identify regulations specific to this type of pesticide in the CFR.

In response to the request that EPA consider another name, the Agency published in the April 23, 1999, issue of the **Federal Register** (64 FR 19958) a document requesting comment on the advisability of substituting an alternative name for the term ''plant-pesticide,'' and requesting appropriate alternative names for this type of pesticide. EPA also specifically requested comment on whether the alternative name, ''plant-expressed protectants,'' would be an acceptable name for this type of pesticide. EPA noted that if the Agency changed the name of such pesticides, the change would only affect the name. It would not affect the status of the pesticidal substance or the genetic material necessary to produce it. Even with a different name, these would still be pesticides under FIFRA section 2(u). Similarly, a change of name would not affect any regulatory requirements.

In response to the April 23, 1999, **Federal Register** supplemental document, EPA received 60 comments. Of these 60 comments, eight comments supported the name ''plant-expressed protectants.'' These commenters argued that the term ''plant-pesticide'' is inappropriate and inaccurate because in standard English it means ''pest killer,'' and many of the pest-resistance mechanisms enhanced by genetic modification do not kill pests in any way, but rather make the crop plants undesirable to pests or not vulnerable to pest attack. These commenters also argued that if plants are labeled as pesticides, a negative connotation could attach to plants. Such plants might be poorly received by the public, and the public perception of a promising branch of science could be tarnished. These commenters also expressed concern that such negative perceptions might lead to labeling requirements or nontariff trade barriers.

Seven comments offered other alternative names without comment on the merit of changing the name. Examples of such names include: Endocides, endogenous bio-control (ebc, or endobio, or endob), enhanced plant protectant, plant protection agent, plant defense agent, plantocides, plendocides, pliocides, intrinsic plant biocontrol agent, intrinsic floral protectant, expressogen, floral defense agent (fda), floral protectant, and gene-transferred protectants.

Eight comments opposed a change of name. These comments, for the most part, thought the name ''plant-pesticide'' appropriate. Some of these commenters argued that the term ''plant-pesticide'' succinctly explains the meaning of the term, i.e., pesticidal

substances introduced into plants. Others arguing for retention of the name ''plant-pesticide'' stated that the term ''pesticide'' does not necessarily have a negative connotation. Several of these commenters asked why the Agency would propose to fix something that is not broken. Several commenters arguing against a change of name stated that EPA should be transparent in its actions, and a pesticide should be called a pesticide. One commenter argued that the term ''plant-pesticide'' has been used by EPA since the early 1990s. It has become a term of art and it would be confusing to change the name. Other commenters stated that if EPA changes the name ''plant-pesticide'' to a more euphemistic name to satisfy one interest group, other interest groups will soon be urging it to change the names of other types of pesticide products to have better marketing potential. These commenters argued against setting such a precedent. Others feared that it would make EPA's effort to control unregistered pesticides more difficult.

Four comments offered alternative names such as Franken-plants, Frankenstein pesticides, Pandora pesticides, products-of-sexual-abuse, alien pesticides, or foreign pesticides.

Among the commenters opposed to a renaming, some also specifically opposed the term ''plant-expressed protectants''. Those opposed to the name ''plant-expressed protectants'' stated that the name obscures the legal issues and attempts to mislead the public into believing that these pesticides are not pesticides at all.

After reviewing all comments, EPA decided to change the name of this category of pesticides from ''plant-pesticides'' to ''plant-incorporated protectants.'' From comments EPA has received both in the comment period on the 1999 supplemental document discussing the possibility of changing the name, and over the years since the 1994 proposed rule was issued, the Agency concludes that many people are not aware of, or do not understand, the FIFRA definition of pesticide. For example, some comments argued that the term ''plant-pesticide'' is inappropriate and inaccurate because it means ''pest killer'' and many pest-resistance mechanisms do not kill pests but rather make the plant undesirable or not vulnerable to pest attack. EPA notes that the term ''pesticide'' in FIFRA section 2 means, in part, ''any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest.'' A pest-resistance mechanism that makes the plant undesirable or not vulnerable to pest attack falls within the definition of pesticide because such mechanisms ''prevent'' or ''repel'' a pest. EPA recognizes that the term ''protectant'' may better describe for the general public pesticides in plants that function by preventing, repelling or mitigating a pest because the term encompasses these concepts, in addition to the concept of destroying a pest. A number of suggested names received in response to the April 23, 1999, **Federal Register**, document utilized the word ''protectant.''

In addition, the name ''plant-pesticide'' appears in some instances to have led some people to believe the Agency is regulating plants, despite the Agency's numerous statements that EPA would not regulate the plant per se, but rather substances within the plant when these were used for pesticidal purposes. EPA recognizes that the name ''plant-pesticide'' may have contributed to this confusion, as some people may interpret the term ''plant-pesticide'' to mean a ''plant that acts like a pesticide.'' EPA believes the adjective ''plant-incorporated'' more accurately conveys the sense that these pesticides are produced and used in the plant. EPA will therefore utilize this adjective in concert with the term ''protectant'' to describe this type of pesticide. EPA chose the adjective ''plant-incorporated'' rather than the adjective ''plant-expressed,'' because the word ''expressed'' represents a technical term of art, and in this instance it appeared preferable to use the term ''incorporated'' which also encompasses a meaning found in the common English dictionary (Ref . 5), i.e., ''joined or combined into a single unit or whole''. The term ''plant-incorporated'' may thus be better understood by the general public than the term ''plant-expressed.''

EPA discounted names received in comments that focus inaccurately on pesticides introduced into plants through genetic modification, e.g., gene-transferred protectants. Names focusing on those pesticides introduced into the plant through the techniques of genetic engineering are too limited, in that such names do not describe the full range of this type of pesticide. This rule addresses pesticides that can be present in a plant because they evolved in the plant, were moved between plants through mating, or were introduced into plants through the techniques of modern biotechnology (e.g., rDNA).

With regard to the concern that other interest groups will soon urge the Agency to change the names of other types of pesticide products to have better marketing potential, EPA recognizes that this may indeed be the case. Indeed, one commenter on the April 23, 1999 **Federal Register** document supplied lengthy comments supporting a name change, and indicating that in the future his organization will suggest that EPA initiate a rulemaking to adopt other terms to describe other products which are regulated under FIFRA. EPA will evaluate each such request on its own merits.

It is not clear to EPA how changing the name of this type of pesticide would affect the Agency's ability to control unregistered pesticides. The comment did not provide a description of how this might occur. As previously stated, the name of the product does not affect the manner in which it is sold or intended to be used, which determines whether a product falls within EPA's jurisdiction under FIFRA.

3. *Does FIFRA apply to pesticides other than traditional pesticides?* EPA does not agree with the contention that FIFRA was meant to regulate only chemical pesticides, such as those extracted from plants or synthesized by petroleum chemistry. The definition of pesticide in FIFRA section 2(u) is not, and has never been, limited to chemical pesticides. Indeed, FIFRA section 2(u) specifically states that a pesticide is any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest, or intended for use as a plant regulator, defoliant or desiccant or a nitrogen stabilizer. Pesticides other than chemical pesticides have been, and continue to be, registered under FIFRA. The first microbial pesticide was registered in 1948 and other biological substances, e.g., pheromones, have been regulated by EPA as pesticides since 1979. Moreover, in 1975, the Committee on Agriculture of the House of Representatives during the debate on the bill (House Report 8841) to extend FIFRA, as amended, for one year, specifically rejected a proposed amendment that would have excluded from the definition of pesticide ''biological parasites, living organisms and predators of pests'' other than microorganisms such as bacteria, fungi or viruses (Ref. 6). Congress again acknowledged in 1996 that the term ''pesticide'' is not limited to chemicals when it enacted FIFRA section 3(c)(10)(B) and established expedited review for both ''biological and conventional pesticides'' (7 U.S.C. 136a(c)(10)(B)). Plant-incorporated protectants, microbial pesticides, biochemicals and semiochemicals (e.g., pheromones) are included under the rubric of biological pesticides.

EPA also does not agree with the implication that risks associated with

pesticide use stem only from the use of chemical pesticides. While EPA believes that as a pesticide class, biological pesticides are more likely to present lower levels of risk, there are certainly chemical pesticides that also fall into the category of ''safer pesticides.'' There may also be biological pesticides, including some plant-incorporated protectants, that could present higher levels of risk.

4. *Why has EPA not implemented a narrower definition of plant-incorporated protectant?* Some comments urged EPA to adopt a more narrow definition of plant-incorporated protectant. These comments include those who urged EPA to define plant-incorporated protectants to be only those pesticidal substances that are introduced into plants from sources outside the plant kingdom, and those who urged the Agency to utilize toxicity to define a plant-incorporated protectant.

FIFRA section 2 defines pesticide broadly as any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest, or intended for use as a plant regulator, defoliant, or desiccant or a nitrogen stabilizer (7 U.S.C. 136 (u)). The FIFRA section 2 definition of pesticide does not make any reference to conditions such as origin nor the level or kind of toxicity that a product must exhibit in order to be considered a pesticide. Instead of defining a substance either in or out of FIFRA based on its toxicity or origin, FIFRA section 25(b) authorizes EPA to exempt pesticides from FIFRA requirements. In the actions it takes today, EPA exempts plant-incorporated protectants derived through conventional breeding from sexually compatible plants. These actions significantly reduce the number of plant-incorporated protectants subject to FIFRA requirements, although they have no effect on the FIFRA section 2 definition of pesticide.

5. *How do substances produced and used in living plants meet the intent standard in the FIFRA definition of pesticide?* EPA received comments indicating some confusion may exist in the broader community regarding the concept of ''intent'' in the FIFRA section 2(u) definition of pesticide, and in how this concept applies to plant-incorporated protectants. One comment, for example, argued that plant defense substances should not be pesticides and stated that by ''strict interpretation of the FIFRA definition of pesticide, substances produced by plants that provide protection against pests and disease cannot be considered pesticides because plants do not 'intend' nor 'produce to protect themselves.''' The commenter went on to state that ''this argument would certainly be correct for wild plants because only natural selection has been involved in stabilization of the character. This argument would also hold for many cases of cultivars improved through breeding programs because many times breeders select for the best yielding plants without specific regard to specific disease or pest; thus there is no intent.''

A key statutory element in the FIFRA definition of pesticide is whether a human ''intends'' that a substance or mixture of substances be used for destroying, preventing, repelling, or mitigating a pest. Just as EPA does not evaluate whether a granule of a traditional chemical pesticide ''intends'' to function as a pesticide in determining whether a substance is a pesticide, the Agency did not base its determination that plant-incorporated protectants are pesticides on the belief that a plant ''intends'' to prevent, destroy, repel, or mitigate a pest. Rather, EPA considers the actions of the humans selling, distributing, or using the substance. To the extent a human relies on a plant's existing pest control properties, the human demonstrates pesticidal intent; if he or she uses, or sells a plant knowing that it typically produces a pesticidal substance he or she ''intends'' for it to be produced. For example, EPA considers that a clear human intent is present when a seller or distributor claims, states, or implies (by labeling or advertising or otherwise) that a substance or organism, either by itself or in combination with other substances or organisms, can or should be used as a pesticide. An example of this would be a company advertising that the cotton seed it is selling would produce cotton plants expressing an insecticidal protein effective against lepidopteran pests. Another example of intent would be a company advertising that a certain variety of squash resists fungal disease.

Yet a third example of a situation where a human displays a pesticidal intent involves a person who sells or distributes a product with actual or constructive knowledge that the product will be used, or is intended to be used, for a pesticidal purpose (see 40 CFR 152.15). EPA considers that the person introducing genetic material encoding a pesticidal substance into a plant displays such an intent. For example, the Bt delta-endotoxin is a well-known insecticidal protein with no other known function; introduction of such a protein into a plant displays a clear pesticidal intent.

Another example of such intent is the use of a name for the product which includes the name of a substance commonly recognized as having pesticidal properties. Such a product will be recognized as a pesticide because the targeted consumer would recognize from the product name that the product contains a pesticide.

A substance in a plant evolving in the wild in response to natural selection is not subject to FIFRA until a human intends the substance to be sold, distributed in commerce, or used to prevent, destroy, repel, or mitigate a pest. Similarly, a cultivar selected, sold and distributed with reference only to yield considerations, without exhibiting any indicia of intent for the cultivar to be used as a pesticide, does not contain substance(s) meeting the FIFRA section 2(u) definition of pesticide. EPA would not treat such a cultivar, or a substance within it, as a pesticide until a human exhibits the requisite intent that the substance(s) or cultivar be used for preventing, destroying, repelling or mitigating a pest.

6. *Why does EPA have a role to play, in light of peer review and existing standards of practice in the plant breeding industry?* Some commenters opposed to EPA's approach argued that use of non-governmental peer review and standards of practice accepted in plant breeding are adequate. As discussed in Unit VII.A.5., whether a substance is a pesticide under the FIFRA section 2 definition depends on the intent of those selling or distributing it. Once something falls within the FIFRA definition of a pesticide, it must generally be registered before it can be sold or distributed in the United States, unless EPA can make the requisite findings to exempt it. For some plant-incorporated protectants, EPA believes that there are circumstances where it is necessary that the Agency employ its statutory authorities to ensure use will not cause unreasonable adverse effects on the environment, and/or ensure that residues of the plant-incorporated protectant can be safely consumed. Some plant-incorporated protectants may be isolated from novel sources (e.g., scorpions, frogs, microorganisms), and may present novel, unknown and/or unfamiliar, toxicological profiles. For example, most of the plant-incorporated protectants reviewed to date by EPA have been insecticidal proteins isolated from microbial sources. These insecticidal proteins are regulated by EPA when they are formulated to be sprayed/dusted on plants. Many of the risk considerations associated with use of the insecticidal proteins in the sprayed/dusted product are present

when the proteins are formulated as a plant-incorporated protectant, even though the route of exposure may be different for the different formulations.

There are also substances that occur naturally in plants, including major crop plants, that can cause toxic effects when present at high concentrations or when presented in novel exposures (Refs. 7 and 8). As these substances could be used as plant-incorporated protectants, EPA believes it is important for the Agency to be able to employ its statutory authorities to ensure use will not cause unreasonable adverse effects on the environment.

EPA, nonetheless, recognizes that plant breeding in the United States has a good record of providing a safe food supply and that plant breeders employ accepted standards of practice to maintain this record. This good record provides support to the Agency's determination that it can exempt plant-incorporated protectants derived through conventional breeding from sexually compatible plants from almost all regulatory oversight, relying only on the post-market reporting of adverse effects. EPA believes that the clarification in this rule that the Agency will not regulate plants per se, in conjunction with the exemption it is issuing today, limits EPA's regulatory role in conventional plant breeding and ensures that the Agency does not unnecessarily supplant the self-regulating aspects of plant breeding.

Some comments that in general otherwise supported EPA's approach, encouraged EPA to ensure that pest resistant crops derived by conventional plant breeding are not subjected to unnecessary regulation. As explained above, EPA believes that its clarification that it would not regulate plants per se, and the exemption it is issuing today, limit EPA's regulatory role in conventional plant breeding and ensures that the Agency does not subject pest-resistant crops derived by conventional breeding to unnecessary regulation.

7. *What were the comments on regulatory procedures?* One comment recommended that, before EPA's regulations are finalized, EPA address issues such as labeling, and field testing and seed production. Another comment recommended that the Agency develop guidelines, in conjunction with the scientific community and industry, to help those who are developing products from these new technologies to determine the factors and situations that might merit regulation by the EPA.

Subsequent to publication of the 1994 **Federal Register** documents, EPA under existing regulations in 40 CFR parts 152 through 173 and 40 CFR parts 177 through 180, took several actions with regard to plant-incorporated protectants. EPA issued, for example, a number of EUPs for field testing of plant-incorporated protectants, exemptions from the requirement of a tolerance for residues of plant-incorporated protectants, and registrations for plant-incorporated protectants.

Together, these actions show how EPA to date has approached labeling, field testing, large scale planting for seed increase, and data needs for evaluating plant-incorporated protectants. In the future, EPA anticipates proposing additional regulations for plant-incorporated protectants that would tailor existing regulations for pesticides so that the procedures would better fit the characteristics of plant-incorporated protectants. Until such regulations can be issued, EPA will continue to apply the regulations in 40 CFR parts 152 through 173 and 40 CFR parts 177 through 180 to plant-incorporated protectants, unless superceded by the regulations published in 40 CFR part 174.

i. *How has EPA approached labeling?* One commenter asked whether labels are expected to appear on bags of seed, and, if so, what information should be on the label. Labeling is generally required by FIFRA for pesticides. Labeling includes both written material accompanying the pesticides and labels on or attached to the pesticide, its container, or wrapper (7 U.S.C. 136 (p)). In its 1994 policy statement for plant-incorporated protectants, EPA attempted to provide the broad outlines of how it would approach labeling. The Agency recognized in the 1994 **Federal Register** policy statement (59 FR 60510) that certain types of labeling which are appropriate for chemical pesticides will not be practical for plant-incorporated protectants. In issuing registrations for plant-incorporated protectants, EPA has followed the labeling regulations at 40 CFR part 156. Under current procedures for plant-incorporated protectants, the pesticide label is held by the producer or the producer's agent(s) and is attached to seed sent to seed propagators. The actual pesticide label requires that informational material must be provided to the farmer with bags of seed sold to farmers. The informational material should indicate that the seed contains a registered plant-incorporated protectant, and its primary purpose is to prevent needless spraying of chemical pesticides. The informational material also conveys any other information pertinent to the grower on the registration and use of the plant-incorporated protectant. Recognizing that the regulations at 40 CFR part 156 were written for chemical pesticides, EPA intends in the future to propose at 40 CFR part 174, labeling requirements specifically tailored for plant-incorporated protectants. No label of any type is required for the plant-incorporated protectants exempted in new 40 CFR part 174.

ii. *How has EPA approached seed increase?* One commenter noted that to produce seed for sale, companies will need to plant significant acreage to generate commercial quantities of seed. The commenter asked how such developmental work will be carried out, as such work does not fall under the traditional usage of an Experimental Use Permit (EUP), because an EUP is granted for generation of data to support registration. Since 1994, EPA issued three ''seed increase'' registrations. Seed increase registrations were issued to allow producers to grow seed for commercial sale, and were limited to seed increase activities. Most registrants, however, currently obtain a registration prior to beginning seed increase activities sufficiently large to produce seed for commercial sale and distribution.

iii. *What is EPA doing in terms of guidance?* With regard to the comment that the Agency develop guidelines to help those who are developing products from these new technologies, EPA, in its November 23, 1994 **Federal Register** policy statement (59 FR 60511), attempted to provide a general perspective on information needs for plant-incorporated protectants. The Agency in the future intends to establish data requirements specific to plant-incorporated protectants through a public notice and comment process. In establishing these testing requirements, EPA will propose the tests it believes are appropriate, indicating the circumstances when each study would be required, conditionally required, or not required. These proposed requirements will be widely available for public comment and will be reviewed in a public meeting of the FIFRA SAP. Amendments can be made to the proposed guidelines as part of the notice and comment process. EPA has already begun this process with the public meetings on December 8, 1999, February 29, 2000 and June 7, 2000 of the FIFRA SAP on data requirements for product identity, human health and non-target organism effects of proteineous plant-incorporated protectants.

8. *What comments were received on the definitions?* Some commenters who supported EPA's approach thought the

plant-incorporated protectant definitions and other associated definitions appropriate. Other comments, while in general supporting the approach, expressed reservations about the definitions. These comments focused primarily on three issues: First, whether the ''genetic material necessary for the production'' should be part of the plant-incorporated protectant definitions; second, clarification of how this term is to be interpreted in several specific circumstances, e.g., with regard to multiple copies of a gene; and, third, what the term ''living'' was intended to signify in the definitions, particularly with regard to regulation of plant-incorporated protectants intended for post-harvest pest control.

i. *Why is EPA including genetic material in the plant-incorporated protectant definitions?* EPA received several comments on including ''genetic material necessary for the production'' in the plant-incorporated protectant definitions. Some comments supported inclusion. Other commenters opposed including genetic material in the definitions for various reasons: First, that inclusion of genetic material in the definition runs counter to the traditional definition of pesticide. Second, commenters disagreed with the presumption that the presence in a plant of genetic material necessary for producing a pesticidal substance indicates a pesticidal intent since the genetic material will still be in the plant when there is no longer any ''pesticidal intent,'' e.g., once a crop has been harvested and regenerative material no longer used for future plantings. Third, commenters argued that including the genetic material necessary for the production in the plant-incorporated protectant definitions is not necessary for EPA to be able to request data on the genetic material. Fourth, commenters asserted that including genetic material in the definitions results in EPA effectively regulating the whole plant because genetic material is found in all parts of the plant. Fifth, commenters alleged that inclusion of the genetic material in the definitions makes EPA's approach inconsistent with policies of the Food and Drug Administration (FDA). Sixth, the comments raised arguments that inclusion of genetic material in the definitions would add an unnecessary layer of complexity to the regulatory process. One commenter suggested that EPA should, on the basis of the above listed considerations, reevaluate EPA's inclusion of the genetic material in the plant-incorporated protectant definitions. The comment suggested that if the Agency concludes that ''genetic material'' must remain in the plant-incorporated protectant definitions, it should be an inert ingredient, not part of the definition of active ingredient.

Based on several considerations, EPA has determined that the ''genetic material necessary for the production'' will continue to be part of the plant-incorporated protectant definitions. First, the conclusion that such genetic material is part of a plant-incorporated protectant is consistent with FIFRA which defines ''pesticide'' broadly, and encompasses both single substances and mixtures of substances intended for preventing, destroying, repelling or mitigating a pest. The genetic material and the substance it encodes for are such a mixture. In this instance, the genetic material is introduced into the plant with the intent to cause a pesticidal effect; i.e., with the intent that the substance(s) produced from this genetic template will ultimately result in a pesticidal effect. Thus, the genetic material, as well as the pesticidal substance, are introduced with the intention of obtaining a pesticidal benefit. Both the genetic material and the pesticidal substance meet the FIFRA statutory definition of pesticide. Second, including the genetic material in the definitions permits EPA to address plant-incorporated protectants during stages of the plant's life cycle or in plant parts (e.g., in pollen or seed) where the pesticidal substance itself is not produced or is produced in amounts below the limits of detection. EPA believes that including the genetic material in the definitions maintains regulatory continuity during such periods in a plant's life cycle and has concluded that this regulatory continuity is important for comprehensively addressing potential risks associated with plant-incorporated protectants within a cohesive and rational regulatory policy. Third, inclusion of the genetic material in the definitions allows the Agency to more readily verify the presence of the plant-incorporated protectant in the plant or plant material because, in many instances, it may be more difficult technically to assay for the substance than it is to assay for the genetic material. Fourth, inclusion of genetic material in the definitions allows EPA to address the spread of the pesticidal substance in the environment through the spread of the genetic material necessary for the production of the pesticidal substance.

a. *Why is inclusion of genetic material in the definition consistent with the traditional use of the term pesticide?* Many of the commenters that disagreed with the inclusion of genetic material in the plant-incorporated protectant definitions argued that including the genetic material runs counter to the traditional use of the term, ''pesticide.''

EPA finds that inclusion of the genetic material in the plant-incorporated protectant definitions is consistent with FIFRA. FIFRA section 2(u) defines the term ''pesticide'' broadly to include ''any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest'' (7 U.S.C. 136 (u)). Section 2(u) defines a pesticide in terms of the intent of humans to exert a deleterious effect upon pests. It does not limit pesticides to substances that directly cause such a deleterious effect (7 U.S.C. 136 (u)). Indeed, EPA has registered chemical substances that do not directly have pesticidal effects but which, when applied to plants, are transformed into the substance having the actual pesticidal effect.

Consistent with FIFRA section 2(u), EPA has concluded that the genetic material necessary for the production of a pesticidal substance, intentionally introduced into a plant, meets the FIFRA statutory definition of a pesticide. Such material is introduced into a plant with the intent of ultimately producing a pesticidal effect even though the genetic material may not itself directly affect pests. The commenter did not identify any specific instances of past Agency usage that would conflict with this conclusion, and EPA is not aware of any.

b. *Why is the genetic material part of the active ingredient definition?* EPA does not agree with the comment suggesting that the genetic material be considered an inert ingredient and not part of the active ingredient. In deciding to include the genetic material necessary for the production of a pesticidal substance in the definition of active ingredient, the Agency considered the statutory definitions of inert and active ingredients. Based on these definitions, EPA concluded that the genetic material necessary for the production of a pesticide fit more closely within the section 2(a) definition of ''active ingredient.'' Section 2(a) defines an active ingredient as, among other things ''the ingredient which will prevent, destroy, repel, or mitigate any pest'' (7 U.S.C. 136(a)(1)). The genetic material is a necessary component of the ability of the plant-incorporated protectant to prevent, destroy, repel or mitigate a pest, as without the genetic material the plant cannot produce the pesticidal substance (See also, 7 U.S.C. section 136(a)(2)). Moreover, the genetic material was inserted with the intention

of obtaining a pesticidal effect: the expression of a substance that will prevent, destroy, repel, mitigate any pest. Consequently, EPA will not define the genetic material necessary for the production of a pesticidal substance as an inert ingredient, as suggested by comment.

c. *How does including genetic material in the definitions relate to EPA's ability to request data?* EPA received comment stating that the Agency has the authority to require all relevant data for a plant-incorporated protectant, including data related to the genetic material, regardless of whether the genetic material is part of the definitions. The same comment noted that deleting the phrase ''genetic material necessary for the production'' from the definitions will not prevent EPA from addressing salient issues related to the spread of genetic material in the environment, or to the levels of the pesticidal substance present in the plant.

EPA agrees that it has broad authority under FIFRA to gather and review data/information on any aspect of a pesticide product or its use in the environment, including data on fate in the environment. However, if a particular aspect of a plant-incorporated protectant is not part of the active or inert ingredient definition for plant-incorporated protectants, it is part of the plant and this rule clarifies that the plant is exempt under FIFRA section 25(b)(1) from FIFRA requirements (40 CFR 152.20). Thus, data gathering considerations are not the primary reason the Agency is including the genetic material in the definitions.

The comment also stated, with regard to EPA's argument that including the genetic material in the definitions permits the Agency to address plant-incorporated protectants during stages of the plant's life cycle where the pesticidal substance itself is not produced, that EPA has the authority to address pesticides at various stages of the product's life cycle, in soil, water and food without including the genetic material in the definitions. EPA agrees that it has the authority to control pesticide residues and the metabolites and degradates of pesticides in the environment and in food. However, as previously noted, unless the genetic material is part of the plant-incorporated protectant, it will be exempt under 40 CFR 152.20. The Agency also believes that in certain circumstances for technical reasons it is easier to identify the presence of the genetic material than the pesticidal substance, and considered this in deciding whether to include the genetic material in the definitions.

d. *Is inclusion of the genetic material in the definitions a disincentive to developers?* The comment provided no specific reason why inclusion of genetic material in the definitions would hinder product development or increase costs. EPA has registered eleven plant-incorporated protectants to date, and including the genetic material in the definitions does not appear to have discouraged companies from developing plant-incorporated protectants.

e. *Is inclusion of the genetic material in the definitions consistent with the assumption of ''intent''?* One commenter opposed EPA's proposal to include the genetic material necessary for production of the pesticidal substance in the definitions of active ingredient and plant-incorporated protectant on the grounds that it is inconsistent with EPA's longstanding implementation of FIFRA, as well as the statute. Specifically, the commenter disagreed with EPA's statement that the genetic material ''is introduced into the plant with the intent that it will ultimately result in a pesticidal effect,'' alleging that this equates the presence of genetic material with pesticidal intent, and fails to acknowledge that a substance can have both pesticidal and non-pesticidal uses, depending on how the substance is intended to be used. The commenter contended that ''once the crop has been harvested and regenerative material removed for future plantings, any genetic material that remains in the food, feed, or other product no longer is accompanied by any 'pesticidal intent.'''

EPA disagrees that its decision to include the genetic material in its definitions of a plant-incorporated protectant and active ingredient fails to adequately recognize the role ''intent'' plays under FIFRA, or that its decision necessarily equates the presence of genetic material with pesticidal intent. The commenter appears to have misunderstood EPA's statements on this issue, and their implications with respect to EPA's regulation of such substances under FIFRA.

As a preliminary matter, EPA believes that including the genetic material necessary to produce a pesticidal substance in the plant-incorporated protectant definitions is consistent with key statutory definitions, as explained at length in Unit VII.B.8.i. FIFRA section 2(u), defines pesticide to include ''any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest'' (7 U.S.C. 136(u)). Under FIFRA, a substance is a pesticide if it is intended to be used for a pesticidal purpose. And as EPA has previously explained, substances that are sold or distributed with the intent that they ''prevent, destroy, repel, or mitigate any pest'' fall within the FIFRA section 2(u) definition of a pesticide. In the absence of other facts indicating a contrary intent, EPA believes that it is reasonable to presume that the introduction into a plant of genetic material that produces, or is intended to produce, a pesticidal substance is clear evidence of a pesticidal purpose. EPA's interpretation is based on the fact that without the genetic material, the pesticidal substance, the substance that will actually ''prevent, destroy, repel, or mitigate any pest,'' cannot be produced by the plant. The sole reason the genetic material is inserted into the plant is to ensure that the pesticidal substance is produced. This is fully consistent with EPA's approach to traditional chemical pesticides (see, 40 CFR 152.15(b)).

However, regulation of the genetic material necessary for the production of a pesticidal substance as an active ingredient or a plant-incorporated protectant in one plant does not mean that some portion of the genetic material cannot be used for another purpose without being subject to FIFRA. At no time has EPA stated that, for example, once a particular promoter is used as part of the construct inserted to produce a pesticidal substance in a plant, thereafter, irrespective of the rest of the genetic construct that is inserted, EPA will always consider insertion of the promoter to demonstrate pesticidal intent. Rather, EPA's statement was intended to clarify that, in the absence of indicia indicating a contrary intent, because the purpose of the introduced genetic material is to produce a pesticidal substance, the insertion of the genetic material will be taken as evidence of a pesticidal intent, and the resulting product will be considered a pesticide under FIFRA. In Unit VII.B.5., EPA discusses in some detail, examples of actions that the Agency interprets as indicia of a pesticidal intent. Clarity on this point is of particular concern with respect to these products because the plant in which the plant-incorporated protectant is contained will remain exempt, and anything that is not part of the plant-incorporated protectant will therefore not be regulated by the Agency under FIFRA.

Thus, EPA agrees with the commenter that under some circumstances the pesticidal intent would cease after harvest, and under such circumstances, the sale of the produce as food or feed would be subject to the FFDCA, rather than FIFRA. The mere presence of such genetic material in the produce will not

cause EPA to treat the produce as a pesticide, absent any indicia of intent to sell, distribute in commerce, or use the produce itself as a pesticide, any more than the presence of traditional pesticide chemical residues renders a food bearing those residues a pesticide. However, if the produce is intended to be used, sold or distributed as containing a plant-incorporated protectant, EPA will regulate it as such. To clarify this, EPA has revised the definition of plant-incorporated protectant, and included a definition of the term ''produce thereof,'' to specifically exclude the products of a plant-incorporated protectant merely bearing ''pesticide chemical residues,'' such as the genetic material, from the definition of a plant incorporated protectant, when the plant-incorporated protectant in the produce is not intended to provide post-harvest control. EPA provides further discussion of its treatment of products that are intended to provide post-harvest control in Unit VII.B.8.iii., and the associated response to comments document (Ref. 2).

The question of pesticidal intent arises in making the determination that the substance being sold or distributed in commerce is a pesticide that must be registered under FIFRA, or whose use is subject to regulation under section 3(a), and for which a tolerance must be granted under section 408 of the FFDCA to permit food or feed bearing the residues of that substance to be introduced into interstate commerce. Unless the Agency is attempting to regulate the produce as a pesticide, the issue of post-harvest control is irrelevant. Thus, as explained in the preceding paragraph, the issue of post-harvest control is essentially irrelevant to EPA's interpretation that the introduction of genetic material into a plant that is expected to ultimately produce a pesticidal effect provides evidence of pesticidal intent, absent any other indicia to the contrary.

In addition, EPA offered in 1994 several reasons in support of its decision to include the genetic material necessary to produce the pesticidal substance, as well as the pesticidal substance, in the definition of a plant-pesticide (59 FR 60521). None of them rested on an assumption that evidence of a pesticidal intent would always be present after harvest.

This approach is fully consistent with the Agency's approach to traditional chemical pesticides. For example, the Agency follows the fate of traditional chemical pesticides in the soil after the harvest of the crop and during rotational crop plantings, even when there is no intent to ''prevent, destroy, repel, or mitigate any pest'' after harvest or during later plantings. This allows EPA, as required by FIFRA, to ensure that a pesticide ''when used in accordance with widespread and commonly recognized practice, . . . will not generally cause unreasonable adverse effects on the environment'' (see 7 U.S.C. sections 136a(c)(5) and 136d). This requirement applies even when the intent of preventing, destroying, repelling or mitigating a pest is no longer evident; for example, as part of its regulation of pesticides EPA considers whether pesticide residues or metabolites can migrate into groundwater, even though there is no intention of obtaining a pesticidal effect from the presence of these substances in groundwater.

f. *How does the genetic material in the definitions relate to the whole plant?* Comments disagreeing with the inclusion of the genetic material in the definitions also argued that including the genetic material ''calls into question EPA's assertion that it has no intention of regulating the plant, since the 'genetic material' will be present in all parts of the plant and in products derived from the plant.''

EPA does not believe that including the genetic material in the definitions calls into question EPA's assertion that it has no intention of regulating the plant. The comment did not explain how regulation of the genetic material would lead to regulation of the whole plant, nor how regulation of genetic material would result in a different outcome in this regard from regulation only of the substance produced from the genetic material. EPA clarifies in this document that plants used as biological control agents are exempt at 40 CFR 152.20. As a result, EPA is not regulating plants or varieties of plants. Rather, the Agency regulates the plant-incorporated protectant (i.e., the pesticidal substance, the genetic material necessary for the production of the pesticidal substance, and any inert ingredient) for use in a particular type of plant (e.g., cotton). To date, EPA has registered several plant-incorporated protectants, and all have been registered for use in the crop, rather than plant variety by plant variety. Moreover, changes to a plant that are unrelated to the plant-incorporated protectant would not be regulated by EPA, but by the United State Department of Agriculture (USDA) and the FDA. For example, changing the color of Bt cotton with the intent of marketing undyed but nonetheless colored cotton would be evaluated by the USDA and FDA (if the cottonseed were to be processed for meal or oil in food or feed uses), even though EPA would evaluate and regulate the effects of the pesticide, Bt.

g. *Is inclusion of the genetic material in the definitions consistent with FDA policy?* One comment suggested that inclusion of the genetic material in the definition of plant-incorporated protectant makes EPA's approach inconsistent with FDA's 1992 Statement of Policy for Foods Derived from New Plant Varieties (57 FR 22984). The comment stated that in its 1992 policy, FDA recognized that genetic material is present in the cells of every living organism and as a result should be presumed to be ''generally recognized as safe.''

EPA disagrees that its approach is inconsistent with the 1992 policy issued by FDA. EPA is publishing elsewhere in this issue of the **Federal Register** an exemption from the FFDCA section 408 requirement of a tolerance, for residues in or on food or feed of nucleic acids that are part of a plant-incorporated protectant. This exemption from FFDCA section 408 requirements applies to the genetic material necessary for the production of a pesticidal substance. Part of the rationale supporting EPA's FFDCA exemption is that nucleic acids are ubiquitous in nature and have always been present in human food and domestic animal feed and have been consumed without harm. This rationale is consistent with FDA's rationale which considers genetic material in food to be ''Generally Recognized as Safe'' (GRAS). EPA believes its approach under FFDCA is consistent with FDA's approach under FFDCA. FIFRA does not automatically exempt substances FDA has classified as GRAS. Instead, FIFRA requires entities who wish to sell or distribute a pesticide to either register the pesticide or seek an exemption from FIFRA requirements prior to such use. For example, garlic used as a pesticide, was registered until EPA exempted it at 40 CFR 152.25(g) as a minimum risk pesticide. Any person may petition EPA to establish an exemption pursuant to FIFRA section 25(b) and FFDCA section 408(d). EPA will make every effort to expedite its review of such petitions.

h. *Does inclusion of the genetic material in the definitions create an overly complex regulatory process?* One comment stated that inclusion of the genetic material in the definitions will result in regulatory uncertainty. The commenter did not explain how inclusion of the genetic material in the definitions would lead to such uncertainty, and EPA assumes that this commenter's uncertainty is related to issues posed by the following questions.

Are all the genes in the vector used to transform the plant covered by the definition? If fragments of a gene are present in the plant, but do not encode a pesticidal substance, are the fragments covered by the definition? Would a producer need to provide EPA with the number of copies of the genes that are introduced into the plant? Would the number of copies be a consideration in the registration process, e.g., in determining when a separate, distinct registration is required? How would changes in regulatory regions affect the status of a registered product; for example, would a new registration be required for a change in a promoter?

EPA does not believe that inclusion of the genetic material in the definitions will lead to an unnecessary layer of complexity in the regulatory process. Because the questions posed by the commenter relate to how EPA views the phrase, genetic material necessary for the production of the pesticidal substance, EPA responds in Unit VII.B.8.ii. to the specific questions posed with regard to the genetic material.

ii. *How is the phrase ''genetic material necessary for the production'' to be interpreted?* EPA's analysis of, and response to, the specific questions posed with regard to the genetic material follows. While conceptually parts of this analysis could apply to exempt as well as non-exempt plant-incorporated protectants, the analysis has practical relevance only for those plant-incorporated protectants that are not exempt from FIFRA requirements and are, or are to be, regulated. For example, the discussion in Unit VII.B.8.ii. on the Confidential Statement of Formula is only relevant to registered plant-incorporated protectants.

a. *How does EPA view genetic material introduced into the plant but not expressed in the plant?* One of the questions posed by comment was whether all the genetic material in a vector used to transform a plant is considered to be part of a plant-incorporated protectant, even if some of the genetic material on the vector is not expressed in the plant and does not play a role in regulation of expression of the pesticidal substance in the plant. A second question concerned the status of gene fragments that do not express a pesticidal substance.

EPA does not intend that all genetic material present in the genetic insert (e.g., in a vector) introduced into the plant must be considered part of the plant-incorporated protectant. EPA defines the term, ''genetic material necessary for the production'' to mean ''genetic material that encodes a pesticidal substance or leads to the production of a pesticidal substance and regulatory regions.'' To more fully describe how EPA interprets this language, two scenarios are discussed.

The first scenario involves sequences that do not function as regulatory regions in the plant but do so in other organisms (e.g., in bacteria). For example, quantities of the genetic material intended to be introduced into a plant are often prepared through fermentation of bacteria containing the desired genetic material on pieces of genetic material called plasmids. To prepare the genetic material, large quantities of bacteria are grown and the plasmids they contain are isolated for subsequent introduction into plant cells. One specific segment of genetic material in these plasmids, called an origin of replication, controls the replication of the plasmids in the bacterium. Even though these origins of replication only function as regulatory regions in bacteria, for technical reasons, they are sometimes part of the genetic material introduced into the plant along with the genetic material that encodes for, or leads to the production of a pesticidal substance. These plasmid origins of replication would not be considered part of the plant-incorporated protectant, because they do not encode for a pesticidal substance nor do they lead to production of the pesticidal substance in the plant, i.e., they do not function as regulatory regions in the plant. Genetic material necessary for vector maintenance/transfer in an intermediate host system (e.g., bacteria) and having no function in the plant would not be considered part of a plant-incorporated protectant. Sequences that function as regulatory regions in one organism (e.g., bacteria), but not in the plant are not ''genetic material necessary for the production of the pesticidal substance'' in the context of a plant-incorporated protectant. These sequences are not used in a living plant, or in the produce thereof.

Under the second scenario, a plant-incorporated protectant is introduced into a plant, but, because of constraints such as the plant's genetic background, or the point of insertion in the plant's genome, or accidents of insertion in which an incomplete copy of a gene is inserted or a regulatory element is lost, the pesticidal substance is never produced from the genetic material. In the absence of pesticidal claims, or other indicia of intent, the genetic material would not be considered part of a plant-incorporated protectant. If, however, in subsequent generations, the previously silent genetic material produces the pesticidal substance, and pesticidal claims or other indicia of pesticidal intent are present, the previously silent genetic material would be considered, along with the pesticidal substance, a plant-incorporated protectant.

b. *Will EPA need to know how many copies of a gene are introduced into a plant?* One commenter questioned whether a registrant would need to provide EPA with the number of copies of the genes that are introduced into the plant when seeking a registration, and whether a change in the number of copies present in the plant would trigger a new registration action.

The number of copies of the gene(s) introduced into the plant for the production of the pesticidal substance will not necessarily be a factor in EPA's determination of whether a new registration is needed. However, the amount of the pesticidal substance (i.e., levels of expression) in various plant tissues may be important for an assessment of potential exposure, and levels of expression may, in some cases, be related to number of gene copies. Thus, while, in general, changes in gene copy number would not automatically require an amendment to the registration, such information may, on occasion, be important in identification and management of risk. Currently, the Confidential Statement of Formula, containing information that must be submitted with each application for registration, describes either the range of levels of pesticidal substance(s) expected to be expressed in the plant, or a maximum level expected to be produced by the plant. Should the level of the pesticidal substance(s) be increased beyond, or decreased below, the range or the maximum level described in the Confidential Statement of Formula, EPA believes that the registrant would generally be required to submit an application for an amended registration pursuant to 40 CFR 152.44, as the risk assessment performed for levels listed in the Confidential Statement of Formula may not be relevant for the new levels. EPA may, in certain cases, waive this requirement, as described in 40 CFR 152.44(b)(1), or permit an applicant to modify a registration by notification or non-notification, in accordance with 40 CFR 152.46. Registrants are therefore encouraged to consult with the Agency in such cases. Distribution or sale of products containing levels beyond those described in the Confidential Statement of Formula may constitute an unlawful act under FIFRA section 12. This approach for plant-incorporated protectants is consistent with the Agency's approach for more traditional

pesticides (e.g., pesticides synthesized through petroleum chemistry) with regard to pesticide levels as described in the Confidential Statement of Formula.

c. *Will EPA need to know about changes in regulatory regions?* One commenter questioned whether changes in regulatory regions would affect the status of a registered product. For example, would a new registration be required if one promoter is substituted for another in an already registered plant-incorporated protectant?

Regulatory regions such as promoters are part of the definition of ''genetic material necessary for the production'' of a pesticidal substance. EPA does not anticipate that a new registration, or an amendment to the existing registration, would always be required with each modification to a regulatory region. However, EPA believes that in general, an application for an amended registration would need to be submitted pursuant to 40 CFR 152.44. Because the Agency has the discretion to waive this requirement, or to permit an applicant to modify a registration by notification or non-notification, registrants are encouraged to consult with the Agency to determine whether the Confidential Statement of Formula would need to be modified and consequently a new registration or an amendment to the existing registration would be required. In some cases a modification to a regulatory region could result in a new formulation, a new use, or a new active ingredient. For example, a change in a regulatory region could result in the pesticidal substance being expressed in a different plant tissue than where the pesticidal substance had been expressed for the original registration. In the assessment for the original registration, risk might only have been evaluated for production of the pesticidal substance in the leaves of the plant. With the change in promotor, the pesticidal substance could now be produced in the fruit, and risk would have to be evaluated for production of the pesticidal substance in the fruit. Evaluations to assess the potential for risk associated with such changes typically occur in a new registration action or an action amending an existing registration.

d. *How will EPA view enzymatic pathways?* Several commenters asked whether EPA would regulate genetic material encoding enzymatic pathways leading to the production of a pesticidal substance. Another comment noted that it ''is not clear from either the definition of active or an inert ingredient how or whether EPA intends to regulate novel gene products, and the genetic material necessary for their production, that represents substances such as enzymes, precursors, or intermediates in biosynthetic pathways that lead to the production of a pesticidal substance.''

With regard to the genetic material necessary for the production of the enzymes that are part of a pathway anabolizing the pesticidal substance, this genetic material is necessary for the production of the pesticidal substance, and thus, it is part of the plant-incorporated protectant.

With regard to the enzymes, precursors, or intermediates in biosynthetic pathways necessary for anabolizing the pesticidal substance, EPA at this time considers them to be part of the plant-incorporated protectant because the substance is intended to ''ensure the presence of the active ingredient''—i.e., it is an inert ingredient. Given that it is theoretically possible that at least some of these substances could be associated with greater potential for adverse effects than the actual substance acting as a pesticide (e.g., precursors could be more toxic to a nontarget species than the actual pesticidal substance), EPA has at this time adopted a prudent course. As the Agency gains greater experience, it may reconsider how it treats enzymes, precursors or intermediates in anabolic pathways introduced with the express purpose of producing a pesticidal effect.

iii. *What comments were received on the word ''living'' in the plant-incorporated protectant definitions?* Several comments suggested that the word ''living'' be deleted from the definition of plant-incorporated protectant because inclusion of that word in the definition of plant-incorporated protectant confused the status of pesticidal substances used for protection against pests post-harvest. For post-harvest control, a pesticidal substance may be produced in the plant during the growth portion of its life cycle, not for protection of the growing plant against pests, but for use during the post-harvest stage, e.g., to protect the seed or fruit during storage. Another comment asked for clarification of the status of exudates and materials that are active in intercellular spaces and/or apoplasts in light of the clause ''for use in the living plant.''

a. *What does the word ''living'' signify in the plant-incorporated protectant definitions?* EPA believes it is important to include the word, ''living'' in the definitions to distinguish plant-incorporated protectants from other types of pesticides. A pesticide is a plant-incorporated protectant only if the pesticide is intended to be produced and used *in situ* in the plant.

The characteristic of being produced *in situ* and used in the living plant makes plant-incorporated protectants unique, particularly with regard to exposure considerations. Exposure considerations for plant-incorporated protectants will be dependent to a large part on the biological characteristics of the living plant in which the plant-incorporated protectant is produced and used. For example, if a plant can outcross with nearby relatives, the potential for spread and increase in the environment of that plant-incorporated protectant through the spread of pollen must be evaluated.

Inclusion of the word ''living'' in these definitions serves to distinguish plant-incorporated protectants from other types of pesticides. For example, it distinguishes plant-incorporated protectants from pesticides like pyrethrum isolated from chrysanthemums and applied to other plants, or pesticides such as the powder, produced by drying and grinding cayenne peppers, dusted on plants with the intent of preventing, destroying, repelling or mitigating a pest. A pesticide that consists of a dead plant or a portion of a dead plant that is intended to be used to control pests is currently regulated under FIFRA as subject to 40 CFR parts 153 through 173 and 40 CFR parts 177 through 180. An example of such a pesticide is pyrethrum, isolated from a plant and applied topically to other plants.

Because of the importance of distinguishing plant-incorporated protectants from other types of pesticides, EPA will retain the term ''living'' in the definitions of plant-incorporated protectant and active ingredient. However, EPA agrees with the commenter that a pesticidal substance produced in the plant during the growth portion of its life cycle, not for protection of the growing plant against pests, but for use during the post-harvest stage, would still be for a pesticidal activity that should be treated by EPA as a plant-incorporated protectant and thus subject to 40 CFR part 174. EPA believes the 1994 **Federal Register** documents (59 FR 60496, 60519, 60535, 60542 and 60545) clearly indicates that this was EPA's intent. However, because EPA does not believe it appropriate to delete the term ''living'' from the definition of plant-incorporated protectant, the Agency clarifies its intent regarding post-harvest control by including the phrase, ''or in the produce thereof,'' in the definition of plant-incorporated protectant.

To reinforce the distinction between plant-incorporated protectants and other types of pesticides, the word ''living'' is

also added to the definition of recipient plant. Similarly, to emphasize that a plant-incorporated protectant is a pesticide produced and used *in situ* in a plant, a definition of ''pesticidal substance'' is added at 40 CFR 174.3 and 40 CFR 152.3.

To further clarify how EPA views a plant-incorporated protectant when the pesticidal substance is produced, or used, in perhaps only part of a plant's life cycle, EPA is including the phrase, ''during any part of the living plant's life cycle,'' in the definition of pesticidal substance. This phrase clarifies that, if a pesticidal substance is intended to be produced and used for preventing, destroying, repelling or mitigating a pest at any time in a plant's life cycle, the pesticidal substance and the genetic material necessary for the production of the pesticidal substance are considered a plant-incorporated protectant, even if the substance is not continually produced at detectable levels throughout all parts of the plant's life cycle, or intended to be used in every part of a plant's life cycle for preventing, destroying, repelling or mitigating a pest. For example, the pesticidal substance may not be produced in the seedling but is produced in the tissues of the mature plant for preventing, destroying, repelling or mitigating a pest. In this situation, the seedling would be considered to contain a plant-incorporated protectant, because the pesticidal substance is produced and used during at least one stage of the plant's life cycle. Further, the genetic material necessary for the production of the pesticidal substance, which itself falls within the definition of pesticide under FIFRA section 2(u), and is defined as part of the plant-incorporated protectant in this rulemaking, would be present during all phases of the plant's life cycle. Depending on the biology of the plant, the life cycle could include, for example, a seed, an embryo, a seedling, a mature or senescent plant.

EPA has broad authority to regulate a pesticide. For example, the Agency follows the fate of substances applied as pesticides in the soil after the harvest of the crop and during rotational crop plantings. This allows EPA, as required by FIFRA, to ensure that a pesticide does not cause unreasonable adverse effects even when the intent of preventing, destroying, repelling or mitigating a pest is not evident.

A plant's life cycle is considered to be one generation, such as a seed to seedling to a mature plant and back to a seed for sexually reproducing plant species, and a vegetative propagule to adult plant to vegetative propagule for plants reproducing asexually. As in the common understanding of the term (Ref. 5), a propagule is the part of an organism that may be disseminated and reproduce the organism.

b. *How does EPA view exudates and materials that are active in intercellular spaces and/or apoplasts?* One commenter requested clarification on the status of exudates and materials that are active in intercellular spaces and/or apoplasts. An apoplast is a cell wall continuum of a plant (Ref. 9). Materials that are active in intercellular spaces are those active between the cells of the plant (Ref. 9). Apoplasts and intercellular spaces are within the living plant. An exudate is composed of substances that were within a plant and were exuded from the plant, within one of the commonly understood meanings of the word exude; i.e.,''to give off gradually through pores'' (Ref. 5). EPA views apoplasts, intercellular spaces and exudates as properly being part of a living plant as described in the 1994 **Federal Register** document (e.g., see 59 FR 60534). EPA believes that this view of a living plant as the sum of its parts is evident in the preamble discussions of the November 23, 1994 policy (59 FR 60496) and proposed rule (59 FR 60519). In order to ensure that this view of the living plant is clear to the regulated community, EPA is adding at 40 CFR 174.3 a definition for the phrase, ''in a living plant,'' which is part of the definition of ''plant-incorporated protectant.'' The definition of ''in a living plant'' is intended to clarify that, for plant-incorporated protectants, the pesticidal substance is part of a plant-incorporated protectant when it is inside the living plant, on the surface of the living plant or an exudate given off gradually as part of a naturally occurring process by a living plant (Ref. 10). The term ''in a living plant'' is defined at 40 CFR 174.3 to mean ''inside the living plant, on the surface of the living plant, or as an exudate from the living plant.'' For the purposes of this rule, EPA defines an ''exudate'' as ''a substance gradually discharged or secreted across intact cellular membranes or cell walls and present in the intercellular spaces or on the exterior surfaces of the plant.'' EPA believes these actions address the commenter's request for clarification.

Sap or other material that is collected through mechanical means from a plant (e.g., sap exuded from a gash resulting from intentional wounding in the bark of a tree) by a human and sold or distributed as a pesticide does not fall within the definition of ''exudate'' because it was not given off gradually as part of a naturally occurring process from the plant. Rather it results from the wounding of the plant. Materials such as maple syrup may meet the definition of ''produce thereof'' if a substance within the syrup is intended to serve a pesticidal purpose by protecting the syrup after it has been collected from the tree. However, sap collected by mechanical means sold or distributed as a pesticide to protect some other produce or thing would be subject to regulations found in 40 CFR parts 150 through 173 and 40 CFR parts 177 through 180, rather than 40 CFR part 174.

iv. *What other modifications have been introduced into the definitions?* EPA, for purposes of clarity, introduces two other modifications to the plant-incorporated protectant definitions. First, EPA modifies the definition of ''plant-incorporated protectant'' for greater clarity, to include the concept of intention to use in a living plant as well as to be produced in a living plant, and to include the concept of the produce thereof, for similar reasons as discussed in Unit VII.B.8.iii.a. ''Produce thereof'' is defined to mean, when used with respect to plants containing plant-incorporated protectants only, a product of a living plant containing a plant-incorporated protectant, where the pesticidal substance is intended to serve a pesticidal purpose after the product has been separated from the living plant. Examples of such products include, but are not limited to, agricultural produce, grains and lumber. Products such as raw agricultural commodities bearing pesticide chemical residues, are not ''produce thereof'' when the residues are not intended to serve a pesticidal purpose in the produce.

Second, the definition of living plant at 40 CFR 174.3 and 40 CFR 152.3 is revised to read:

Living plant means a plant, plant organ or plant part that is alive, viable or dormant. Examples of plant parts include, but are not limited to, seeds, fruits, leaves, roots, stems, flowers and pollen.

v. *What is an inert ingredient for this type of pesticide?* EPA originally proposed to define inert ingredients for plant-incorporated protectants as ''any substance, such as a selectable marker, other than the active ingredient, and the genetic material necessary for the production of the substance, that is intentionally introduced into a living plant along with the active ingredient, where the substance is used to confirm or ensure the presence of the active ingredient'' (59 FR 60521).

In this section, EPA focuses on selectable markers. EPA discusses other inert ingredients in Unit VIII.B.8.ii.d. Therefore, throughout this discussion,

EPA uses the phrases ''substances used to confirm or ensure the presence of a plant-incorporated protectant in a plant'' and ''selectable markers'' interchangeably. Selectable markers are genetic material introduced into the plant or plant cells concomitant with the genetic material that confers the desired trait (e.g., a pesticidal trait). A selectable marker provides a means of distinguishing and selecting plants or plant cells that have successfully incorporated the genetic material conferring the desired trait from the vast majority of plants or plant cells that have not. For example, the selectable marker may endow the recipient cell with the ability to resist a lethal agent and the selection process may depend upon the cells that acquired the introduced genetic material being resistant to the lethal agent. When the cells are exposed to the lethal agent, the cells that did not incorporate the genetic material are killed, while the cells that did incorporate the introduced genetic material survive. When the researcher uses the toxic agent to select those cells that can resist the lethal agent, the researcher also selects the cells that acquired the desired trait (e.g., a pesticidal trait).

In response to its proposed rule in 1994, EPA received several comments suggesting that plant-incorporated protectant inert ingredients that had been reviewed by FDA should be exempt from EPA review. One commenter, noting that the 1992 FDA policy statement (57 FR 22984) addresses the relevant food safety issues associated with selectable markers, suggested these should only be reviewed by FDA. Other commenters suggested that the genetic material necessary for the production of the pesticidal substance be defined as an inert ingredient for plant-incorporated protectant, along with selectable markers, rather than as an active ingredient. Yet other commenters suggested that EPA broaden its original proposed rule to include ''a substance used to assist in the identification of plants or plant cells containing the active ingredient.'' Another commenter suggested that marker genes and their products should be considered active ingredients in order to ensure some type of ''safety review'' of the marker genes. Another commenter urged EPA to make clear that plant-incorporated protectant inert ingredients are excluded from EPA's ''new inerts'' policy (52 FR 13305, April 22, 1987) which requires testing and EPA approval of inerts not already on the Agency's approved inerts list.

During development of the final rule, EPA reconsidered its 1994 proposed rule and published a supplemental document on July 22, 1996 in the **Federal Register** (61 FR 37891), discussing the Agency's treatment of inert ingredients. In the supplemental document, EPA discussed several considerations that argued against treating selectable markers as inert ingredients, including: the unique nature of plant-incorporated protectants and substances such as selectable markers; the function of selectable markers in plants; and the effects of selectable markers on the performance of the plant-incorporated protectant. The Agency pointed out that substances such as selectable markers are intentionally introduced into plants to aid in the selection of plants or plant cells that contain the desired genetic material necessary for producing the plant-incorporated protectant and consequently are typically introduced into the plant at the same time as the active ingredient (61 FR 37892–37893, July 22, 1996). Because the requisite intent to include such substances in the pesticide product is present in the use of selectable markers in plant-incorporated protectants, the markers would be considered to be an inert ingredient under the Agency's traditional interpretation of that term. But EPA also noted that selectable markers do not have pesticidal properties themselves, are not necessary for the plant-incorporated protectant to function in the plant and are usually used only once in the early stages of product development, and are of no use in modifying or enhancing the pesticidal activity of the plant-incorporated protectant. EPA also speculated that the marker genes could be lost from the plant during subsequent breeding with no effect on the active ingredient, and provided the public an additional opportunity to comment on how such substances should be viewed under FIFRA (61 FR 37893, July 22, 1996).

Many of the comments EPA received in response to the supplemental document recommended that selectable markers not be considered inert ingredients. Several of these commenters supported their recommendation by noting that it would reduce the ''potential for duplication with reviews by the FDA,'' which already reviews the food and feed safety of selectable markers. One commenter, who supported a decision not to consider all selectable markers as inert ingredients, nevertheless noted that the commenter was ''particularly concerned about adverse environmental impacts of such substances on non-target organisms, particularly salmon or members of aquatic ecosystems upon which their survival depends.'' Another commenter, while concurring that EPA should not regulate selectable markers as inert ingredients, suggested that EPA explore in greater detail the ramifications of using herbicide tolerant traits as selectable markers. This commenter was concerned that potentially widespread use of herbicide resistance traits as selectable markers ''may tempt unscrupulous farmers to apply the herbicide to crop plants in the field, even though the herbicide is not registered for use with the crop plant.''

To determine how to proceed, the Agency considered the comments received in response to both its original proposed rule and the supplemental document, and the degree to which they addressed the considerations laid out in the supplemental document. This included comments on the Agency's treatment of individual selectable markers, as well as the Agency's overall approach to inert ingredients. None of the comments, however, provided information or analyses that definitively resolved the question one way or another.

Although the majority of commenters supported a decision not to treat selectable markers as inert ingredients, most of these comments appeared to be based on concerns over the potential for duplicative oversight between EPA and FDA. In addition, several comments received in response to both notices raised human health and environmental safety issues surrounding certain selectable markers, such as genes coding for herbicide or antibiotic resistance, and supported some government oversight to ensure that a ''safety review'' was conducted.

With respect to the potential for duplicative oversight, EPA acknowledges that some degree of overlapping jurisdiction with FDA currently exists in that both agencies share responsibility for evaluating different aspects of a selectable marker. As previously explained, both agencies have agreed that EPA will address under its regulatory jurisdiction the food safety issues associated with the pesticide, including selectable markers. Any food safety questions beyond those associated with the pesticide, such as those raised by unexpected or unintentional compositional changes, are under FDA's jurisdiction (57 FR 22984 and 59 FR 60514).

Bearing in mind the concerns with respect to duplicative review, EPA considered whether relinquishing

jurisdiction to FDA would best address the health and safety concerns raised. Although many of the issues with respect to the safety of the food or the development of antibiotic resistance are within FDA's traditional purview and expertise, the issues with respect to impact on non-target organisms and ecosystems are ones with which EPA has greater experience in regulating under FIFRA. And given EPA's longstanding expertise in considering food safety concerns under the FFDCA, it was determined that on balance, the totality of the concerns could be better addressed by regulating under both FIFRA and the FFDCA than by regulating under the FFDCA alone. These considerations thus weighed in favor of considering selectable markers to be inert ingredients in a plant-incorporated protectant. Moreover, EPA and FDA can work together to minimize the impacts arising from any overlap in jurisdiction, and will coordinate extensively towards that end.

As EPA explained in the 1996 supplemental document, FIFRA and FFDCA contain only general definitions of the relevant terms. FIFRA section 2(u) defines a ''pesticide'' as any substance or mixture of substances intended ''for preventing, destroying, repelling, or mitigating any pest'' or ''for use as a plant regulator, defoliant, or desiccant'' or ''any nitrogen stabilizer (7 U.S.C. 136(u)).'' An ''active ingredient'' is defined as ''in the case of a pesticide other than a plant regulator, defoliant, desiccant, or nitrogen stabilizer, an ingredient which will prevent, destroy, repel, or mitigate any pest'' (7 U.S.C. 136(a)). FIFRA defines ''inert ingredient'' to mean ''an ingredient which is not active'' (7 U.S.C. 136(m)). Under the FFDCA, a substance is a ''pesticide chemical'' if it is ''a pesticide within the meaning of [FIFRA], including all active and inert ingredients of such pesticide'' (21 U.S.C. 321(q)(1)).

Although the statutory definitions provide some guidance, they do not definitively resolve whether the Agency should define substances intentionally introduced into the plant with the active ingredients as inert ingredients. EPA's current pesticide regulations, along with EPA's past practice and interpretation of those regulations, however, although not specifically addressing selectable markers, do provide considerable insight into the issue of inert ingredients. EPA's longstanding regulatory definition of ''inert ingredient'' includes as an inert ''any substance (or group of structurally similar substances if designated by the Agency), other than an active ingredient, which is intentionally included in a pesticide product'' (40 CFR 152.3(m); see also 40 CFR 158.153(f)). A ''pesticide product'' is defined by regulation to be ''a pesticide in the particular form (including composition, packaging, and labeling) in which the pesticide is, or is intended to be, distributed or sold'' (40 CFR 152.3(t)).

These definitions capture as inert ingredients, all those substances that are intentionally included in the pesticide product that are not active. Further, EPA has consistently interpreted these definitions to include substances that serve no useful purpose in the product. The Agency has never required that inert ingredients have pesticidal properties themselves, nor has the Agency required that inert ingredients modify or enhance the pesticidal activity of the pesticide although inert ingredients are often used for at least one of these purposes. In fact, the Agency has indicated on several occasions that inert ingredients are generally not ''pesticidally active'' (See, e.g., Inert Ingredients in Pesticide Products; Policy Statement, (52 FR 13305, April 22, 1987); see also Pesticide Registration Procedures; Pesticide Data Requirements, (53 FR 15952, 15963, May 4, 1988)). Thus, the essential criterion that the Agency has used to determine whether an ingredient is an ''inert'' is the intent of the producer to include the substance in the pesticide product.

In the case of plant-incorporated protectants, the Agency has emphasized in both the 1994 proposed rule and the 1996 supplemental document that substances ''such as selectable markers are intentionally introduced into plants'' (61 FR 37892–37893; see also 57 FR 60521). In the 1996 supplemental document, the Agency pointed out that substances such as selectable markers are intentionally introduced into plants to aid in the selection of plants or plant cells that contain the desired genetic material necessary for producing the plant-incorporated protectant and consequently are typically introduced into the plant at the same time as the active ingredient (61 FR 37892–37893). Because the requisite intent to include such substances in the pesticide product is present in the use of selectable markers in plant-incorporated protectants, the markers would be considered to be an inert ingredient under the Agency's traditional interpretation of that term. No commenters provided information or analyses that would contradict this interpretation or that would lend support to the other considerations laid out in the 1996 notice arguing against treating these markers as inert ingredients.

Moreover, since the 1994 proposed rule and 1996 supplemental document, EPA has had experience with selectable markers in the registration of several plant-incorporated protectants that is relevant to the considerations presented in the 1996 supplemental document. For example, contrary to the speculation in the 1996 document, some selectable markers are not used only once, i.e., to distinguish the cells transformed with the pesticidal trait from those that had not acquired the trait. Rather, the ability to resist the lethal agent is being used during the breeding process to develop commercially viable lines as a phenotypic identifier to select progeny plant lines having the desired pesticidal trait. In such cases, the role played by the selectable marker is somewhat different than was considered in 1996. In addition, in the interim, EPA has become aware of other substances that could be used as selectable markers, e.g., green fluorescent protein (Ref. 11), and while EPA can make some prediction about the potential interactions with and effects on the pesticidal substance of currently used selectable markers, e.g., antibiotic and herbicide resistance, it cannot do so for selectable markers that may be developed and used in the future.

In light of this experience, and in light of the concerns raised by some of the commenters regarding safety issues associated with the use of selectable markers, the Agency believes it prudent to consider these substances to be inert ingredients and to continue to assess their safety. EPA believes that these considerations outweigh the considerations discussed in the 1996 supplemental document, arguing against treating such substances as inert ingredients. Moreover, to ensure that health and safety issues are addressed by the Agency with the greatest technical expertise without duplicative oversight, EPA and FDA will work closely to address areas of potentially overlapping jurisdiction, and to share expertise in reviews. Consequently, for these reasons, as well as for the reasons outlined in the 1994 proposed rule, the Agency has determined that it will adopt the definition it proposed in 1994 with minor modification.

One comment asked whether EPA intended to treat the enzymes leading to the production of the pesticidal substance as inert ingredients. As noted in Unit VII.D.8.ii.d., EPA will consider the enzymes, precursors, or intermediates in biosynthetic pathways necessary for anabolizing the pesticidal

substance to be an inert ingredient of the plant-incorporated protectant.

One comment suggested that in ''anticipation of inerts that would be introduced to perform other nonpesticidal functions, the restrictive language should be removed and the relationship to the active ingredient characterized as intentionally introduced into a living plant in association with the active ingredient.'' EPA disagrees. The commenter's suggested language is so broad that it would cover introduced genetic sequences that EPA considers to be appropriately within USDA's or FDA's sphere, e.g., modifications to the starch content of a potato. As noted in the preceding paragraph, EPA anticipates that as it gains experience, it may change its view of what is appropriately an inert ingredient for plant-incorporated protectants, although the Agency does not anticipate that it would subsume in its definition all modifications affecting substances that have traditionally been in USDA's or FDA's purview. EPA acknowledges that any modification of the definition of inert ingredient for plant-incorporated protectant would be made through rulemaking.

With regard to the comment urging EPA to make clear that plant-incorporated protectant inert ingredients are excluded from EPA's ''new inerts'' policy (52 FR 13305), EPA has created 40 CFR part 174, subpart X, specifically for inert ingredients for plant-incorporated protectants. Inert ingredients in 40 CFR part 174, subpart X, are not part of EPA's ''new inerts'' policy (52 FR 13305) per se; however EPA's approach for plant-incorporated protectants is consistent with the policy.

Several commenters requested that EPA consider the genetic material necessary for the production of the pesticidal substance to be an inert ingredient. For reasons described in Unit VII.B.8.i., EPA will not consider this genetic material to be part of the inert ingredient.

C. Clarification of Exemption at 40 CFR 152.20; Status of Plants Used as Biological Control Agents with Regard to FIFRA Requirements

Most comments supported EPA's proposal to clarify that, although plants used as biological control agents will remain exempt under 40 CFR 152.20, plant-incorporated protectants will not fall within that exemption, but will be subject to FIFRA requirements, including the regulations codified at 40 CFR part 174. However, some commenters argued that the ability to resist pests is a characteristic of the plant and should not for regulatory purposes be separated from the plant itself. Another comment opposed exempting plants from FIFRA requirements and argued that the definition of biological control agent at 40 CFR 152.3 does not apply to plants. This commenter argued that the definition at § 152.3 was meant to apply to classical biological control agents—predaceous and parasitic arthropods—whose sole use is to control pests. The commenter further argued that plants cannot be considered classical biological control agents because the primary use of plants is not pest control but yield of a product; pest control for plants is merely an attribute which helps to achieve yield.

With regard to the comment concerning ''classical biocontrol agents,'' EPA recognizes that classical biocontrol generally involves the use of one organism such as a predaceous or parasitic arthropod to protect another organism such as a plant (Refs. 10 and 12). Plants were not specifically addressed in the regulation EPA published in the June 2, 1982, **Federal Register** document (47 FR 23928) that exempted, under FIFRA section 25(b)(1), most biological control agents from the requirements of FIFRA. There are, however, circumstances in which plants are used as ''classical'' biological control agents analogous to the use of predaceous and parasitic arthropods to protect other organisms. For example, organic gardeners use living plants, such as marigolds, chrysanthemums and geraniums, in their gardens with the intent of protecting other plants, such as vegetable plants. This type of plant for this type of use clearly meets the 40 CFR 152.3 definition of biological control agent because it is a ''living organism applied to or introduced into the environment that is intended to function as a pesticide against another organism declared to be a pest by the Administrator.''

Plants, when humans intentionally use them for preventing, destroying, repelling or mitigating a pest, meet the FIFRA section 2(u) definition of pesticide, and thus are pesticides. A living plant that is intended to have a pesticidal effect meets the definition at 40 CFR 152.3 of biological control agent because it is a ''living organism applied to or introduced into the environment that is intended to function as a pesticide against another organism declared to be a pest by the Administrator.'' In 1994, EPA advised the public that the Agency considered plants that protect themselves against pests to fall within the definition of biological control agents (59 FR 60496). This statement created some uncertainty regarding the regulatory status of such plants under FIFRA, in part because such plants were not explicitly addressed in the preamble to either the proposed or final rule establishing the exemption at 40 CFR 152.20 (46 FR 18, 322, March 24, 1981; 47 FR 23928, June 2, 1982). Today's action clarifies the status of such plants. The plants themselves will remain exempt, but EPA will continue to regulate the pesticidal substances in such plants under FIFRA and the FFDCA, even when they are intended to be used in the exempt plants.

Moreover, the commenter fails to provide any meaningful distinction between ''predaceous and parasitic arthropods whose sole use is to control pests'' and plant-incorporated protectants. All agricultural use pesticides are, in some sense, applied to crops to increase yields, or to otherwise obtain the maximum profit from the crop. It has been EPA's experience that farmers do not apply pesticides simply to kill insects without also intending to affect yield, or to otherwise protect or increase a crop's profitability.

EPA also disagrees with the comment that, for regulatory purposes, a characteristic of the plant should not be separated from the plant itself. EPA believes that its decision to regulate plant-incorporated protectants, while exempting the plants themselves is an appropriate regulatory approach because it allows the Agency to focus its oversight on the ''pesticidal'' characteristics of the plant, and any associated risks. In addition, this approach is consistent with the Agency's long-standing regulation under FIFRA.

Under existing regulations, although the plant itself is exempt from FIFRA requirements, substances that are extracted from plants and used as pesticides are not similarly exempted. For example, chrysanthemums produce pyrethrum, a substance that has insecticidal activity. Chrysanthemums that produce pyrethrum are exempt from regulation when used as biological control agents (i.e., living chrysanthemums), but pyrethrum itself as the pesticidal substance, is not exempt when it is extracted from chrysanthemum plants and applied to other plants as a pesticide. This distinction is reasonable in light of the potential for increased and unique exposures due to large-scale application of extracted pyrethrum to plants that do not naturally produce it. The use of extracted pyrethrum as an insecticide can involve exposure to the pesticide over large acreage, whereas the exposure

associated with pyrethrum produced by living chrysanthemum plants would not be expected to reach such proportions. In addition, application of pyrethrum beyond the environment in which it is naturally produced (i.e., beyond the living chrysanthemum plant) could result in new or unique exposures of nontarget organisms, including humans.

With the development of modern biotechnology, the number of such plants sold with the intention that the pesticidal substances in the plant function while in the plant, rather than extracting the pesticidal substance from the plant, have dramatically increased. But of greater regulatory significance, with these techniques, a plant can be endowed with properties that were previously not possible; for example, the ability to produce pyrethrum can be given to a crop plant such as corn. Different exposure considerations would exist for pyrethrum in corn than for pyrethrum in chrysanthemums. Given that millions of acres are planted to corn in the US, some of the exposure considerations of pyrethrum in corn might be more analogous to the considerations for exposure from sprayed pyrethrum than to considerations for pyrethrum in chrysanthemums.

Similarly, potato, cotton and corn plants have recently been engineered to produce the endotoxin from the bacterium, *Bacillus thuringiensis* (Bt). EPA assessed the risk of these Bt-based plant-incorporated protectants in a manner consistent with EPA's treatment of Bt in other formulations. Bt is regulated under FIFRA when formulated in products to be dusted/sprayed on plants for protection against pests. Many of the risk considerations evaluated for Bt used as a plant-incorporated protectant are the same considerations evaluated for Bt sprayed or dusted on plants as a pesticide.

In this final rule, EPA clarifies that plants that humans use with the intention of controlling pests will remain exempt from FIFRA requirements pursuant to the exemption at 40 CFR 152.20, but that the pesticidal substances, and inert ingredients contained in the plants, remain subject to the requirements of FIFRA, as codified at 40 CFR part 174. The regulatory text at § 152.20 is also modified to make clear that the exemption for plants used as biological control agents applies to living plants and does not apply to plants or plant parts that have, for example, been dried or processed for use as pesticides. An example of this latter type of pesticide would be the powder, produced by drying and grinding cayenne peppers, dusted on plants with the intent that it would protect the plants against disease. This type of pesticide does not meet the definition of biological control agent and is not exempted at § 152.20. Processed plants or plant parts used as pesticides are currently subject to the regulations at 40 CFR parts 150 through 173 and 40 CFR parts 177 through 180.

EPA believes it is appropriate to exempt the living plant from FIFRA requirements. The Agency believes its focus on the plant-incorporated protectant rather than on the plant allows it to ensure a low probability of risk to humans and the environment, while imposing a minimum burden on the development of plants containing novel plant-incorporated protectants and conserving limited Agency resources. Had EPA chosen to regulate the plant, it would have issued registrations for plant varieties. By focusing on plant-incorporated protectants, in contrast, EPA can issue a registration for use of the plant-incorporated protectant within a larger grouping, such as a crop. This allows the Agency to focus its resources on evaluating the pesticidal properties of the plant, rather than on other properties of the plant. EPA believes that the clarification in this rule today that it will not regulate plants per se, and the exemption it is issuing today in another section of this document, and in a companion document published elsewhere in this issue of the **Federal Register**, limit EPA's effect on plant breeding and allow most aspects of plant breeding to be pursued without EPA regulation.

However, EPA also believes it is appropriate to exclude certain plant-incorporated protectants from the exemption at 40 CFR 152.20. Section 25(b) requires the Agency to support its determination that a class of pesticides meet the standard for an exemption. EPA's assessment supporting the 1982 exemption did not encompass all of the plant-incorporated protectants being developed and marketed today, and the Agency could not rely on those assessments to support such an exemption. As noted above, with modern biotechnology, a plant can be endowed with properties that were not possible in 1982, and different exposure and hazard considerations would exist for such plants. Nor could the Agency develop sufficient evidence to maintain a categorical exemption for all plant-incorporated protectants, given all of the possible genetic modifications that can be achieved with these techniques, even if the Agency were inclined to do so. As an initial matter, Agency could not anticipate all potential modifications, let alone develop a risk assessment for all potential intended, and unintended, effects from such modifications.

EPA is exempting those plant-incorporated protectants for which the Agency can support the necessary findings, based on the available scientific evidence and the Agency's technical expertise. For example, the exemptions established in another section of this document, and in a companion document published elsewhere in this issue of the **Federal Register**, encompass the chrysanthemum discussed above, as long as it meets the exemption criteria, even though it contains a plant-incorporated protectant. As the Agency's base of knowledge and experience increases, exemptions for additional categories of plant-incorporated protectants may be warranted. But until then, the Agency believes that a case-by-case review of plant-incorporated protectants not specifically exempted in this rule, is necessary to ensure that such products can be sold and used without generally posing unreasonable adverse effects on the environment. Case-by-case review will also allow the Agency to increase the available body of scientific knowledge and experience to determine whether additional exemptions are warranted. In addition, any person may petition EPA to establish an exemption pursuant to FIFRA section 25(b) and FFDCA section 408(d). EPA encourages additional exemptions when supported by scientific data and will make every effort to expedite its review of such petitions, consistent with the requirements of these sections.

D. Exemption of Plant-Incorporated Protectants Derived Through Conventional Breeding from Sexually Compatible Plants

This rule exempts from FIFRA requirements, except for the adverse effects reporting requirements at 40 CFR 174.71, plant-incorporated protectants derived through conventional breeding from sexually compatible plants.

In 1994, EPA proposed to exempt from all FIFRA requirements, except for the adverse effects reporting requirements now at 40 CFR 174.71, a category of plant-incorporated protectants based on the premise that new exposures would be unlikely if the genetic material leading to the production of the plant-incorporated protectant is derived from a plant closely related to the recipient plant. EPA offered three options for defining plant-incorporated protectants derived from plants closely related to the recipient plant. All of the options were

based on the concept of source organism and the phylogenetic relatedness of the genetic donor and recipient. None of the three options was based on the process by which a plant-incorporated protectant was introduced into the recipient plant. Option 1, based upon sexual compatibility, was EPA's preferred option (59 FR 60534). Under this option, plant-incorporated protectants derived from plants sexually compatible with the recipient plant would be exempt from FIFRA regulation. Options 2 and 3 used taxonomy (genus) to define closely related plants, either exclusively (Option 2) or in conjunction with sexual compatibility (Option 3). The Agency also requested comment on the utility of an exemption criterion based on the process (e.g., rDNA) used to introduce the plant-incorporated protectant into a plant (59 FR 60514 and 60530). This approach was discussed by the SAP Subpanel and BSAC Subcommittee at the joint meeting of these scientific advisory groups held on January 21, 1994. In this approach, plant-incorporated protectants developed through techniques other than those of modern biotechnology would be exempted, e.g., those developed through conventional plant breeding would be exempted. Categories of those plant-incorporated protectants that were not exempted by this criterion could subsequently be considered for exemption on the basis of risk potential.

The joint subcommittee/subpanel report recommended such a ''process-based'' approach on the following three considerations. First, the National Institutes of Health Guidelines for Research Involving Recombinant DNA Molecules established a precedent that has worked well. Second, although new techniques, such as rDNA, are more precise than conventional plant breeding, it is possible to make with rDNA novel genetic modifications never before possible. The novel combinations possible with modern genetic techniques create uncertainties about how the gene will function and how its products may affect the plant's phenotype and its impact upon the environment and human health. Third, establishing rDNA methodologies as a criterion for oversight may give the public more confidence that risk potential is being evaluated. As a result, approved products may move to the marketplace more easily (Ref. 15).

The majority of the comments on the proposed exemption based on the degree of relatedness between the donor and recipient plants favored the option based on sexual compatibility between the donor and recipient plants (preferred option in the November 23, 1994 **Federal Register** document (59 FR 60533)). The Agency did not receive any comments that favored the option based on taxonomy, Option 2. Although several comments favored the option that relied on both taxonomy and sexual compatibility, Option 3, EPA also received comments that expressed reservations about using taxonomy to describe a close degree of relatedness for regulatory purposes.

EPA received numerous comments supporting an approach based on process, i.e., that those plant-incorporated protectants introduced by rDNA would be regulated. The arguments advanced by these commenters can be represented by the comment that:

> genetic engineering (particularly recombinant DNA [rDNA] methodologies), represent a fundamental technical advance over traditional plant breeding in the ability to manipulate plants genetically. Genes which code for production of plant-pesticides can be readily turned 'on' or 'off' to dramatically increase the existing levels of plant-pesticides within plants, turning plants into pesticide factories and delivery systems. . . . 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. 13).

Several letters described quantitative changes in the levels of plant-incorporated protectants as specific instances in which the commenter believed risk would be better addressed by an approach based on process.

Some comments urging regulation based on whether rDNA had been used to introduce the plant-incorporated protectant supported exempting conventional breeding. One commenter, for example, stated that pesticidal products that ''are introduced by traditional breeding pose generally low risk and should be exempt'' (Ref. 14).

Based on the advice of the BSAC and SAP at the joint meeting held January 21, 1994, and the comments received in response to the November 23, 1994 **Federal Register** document, EPA has determined that it is appropriate to issue a limited exemption for those plant-incorporated protectants derived through conventional breeding from plants sexually compatible with the recipient plant. In a companion document published elsewhere in this issue of the **Federal Register**, EPA solicits public comment on alternate options for the category of plant-incorporated protectants derived through modern biotechnology, e.g., rDNA techniques, from plants sexually compatible with the recipient plant. The Agency is considering these options in response to the public comment received on its earlier proposals. One of these options would establish notification procedures, and as the public has not had an opportunity to comment on either the procedures themselves, or the criteria on which EPA would base its regulatory decisions, the Agency believes it is appropriate to seek additional public comment prior to adopting a particular option. In addition, as these alternatives would distinguish between categories of plant-incorporated protectants based solely on the processes by which they are derived, the public will also have an opportunity to present additional comments on whether this is an appropriate distinction for regulatory purposes.

1. *What is the language of the exemption?* In this action, EPA is exempting only a subgroup of the category it proposed to exempt in 1994, those plant-incorporated protectants derived through conventional breeding from sexually compatible plants.

i. *Why is sexual compatibility an appropriate standard?* EPA believes sexual compatibility is an appropriate standard because sexually compatible plants share a common pool of genetic material, even though there may be some variability among plants in sexually compatible populations. Sexual compatibility, the ability to produce viable offspring, is only possible in nature for plants that possess many traits in common. Traits, and the genetic material encoding them, can be passed through sexually compatible plant populations by hybridization, and the mixing of genetic material that occurs through this process of mating tends to a situation where the members of sexually compatible population have similar traits and similar genetic material. This is particularly true with crop plants where generations of selection and breeding have tended to decrease the total genetic variability in many agronomic species. Sexually compatible thus presents a natural grouping of plants which can be readily described and used as a regulatory standard, and about which a large amount of information exists in the scientific literature. This information can be used in assessing risk.

Using sexual compatibility as a standard affords a clear delineation of whether a plant-incorporated protectant meets the conditions of the exemption. In most cases, whether two plants are sexually compatible is known; thus, testing to determine whether the plants

are sexually compatible is not likely to be necessary. If, in rare cases, it is not known whether two plants are sexually compatible, the means of determining sexual compatibility is straightforward and simple. Sexual compatibility is empirically demonstrable. EPA believes that the criterion of sexual compatibility provides a high level of regulatory clarity and the greatest ease of implementation, while at the same time presenting the lowest probability of novel dietary exposure. This standard allows the public, industry, and EPA to easily and readily identify those plant-incorporated protectants that meet the criterion of being derived from plants closely related to the recipient plant.

a. *Why is sexual compatibility limited to conventional breeding?* As explained in a companion document published elsewhere in this issue of the **Federal Register**, EPA is soliciting additional comment on the various options it is considering in response to the significant comments it has received raising issues specific to plant-incorporated protectants derived through genetic engineering. Because none of the comments raised significant issues relative to plant-incorporated protectants derived through conventional breeding, the Agency is finalizing its proposals with respect to this subgroup of products. Therefore, EPA includes in the definition of sexually compatible at 40 CFR 174.3 the clause ''through conventional breeding.'' EPA also provides a definition of conventional breeding that equates it to 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 any of the following technologies: 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. EPA believes that this definition addresses the recommendation of the SAP/BSAC at the January 21, 1994 joint meeting that ''the Agency define methodologies in a way that clearly delineates to the scientific community and the public what is and is not included in the regulatory scope'' (Ref. 15).

In the 1994 proposed rule (59 FR 60524) EPA states that its proposed rule is based on ''experience with the exposure of human populations to crops developed through the breeding process, i.e., crops developed through 100 years of scientific breeding among sexually compatible plant populations using Mendelian genetics.'' In its 1994 proposed rule, EPA calls this type of breeding, ''traditional breeding'' (see e.g., 59 FR 60519). When the Agency determined that it would exempt a subgroup of plant-incorporated protectants in the sexually compatible grouping while allowing additional comment on how EPA should treat those plant-incorporated protectants introduced into the plant through the techniques of modern biotechnology, EPA chose to describe the exempt group in the most straightforward manner; i.e., those derived through breeding. Recognizing that many consider the modern techniques of biotechnology as simply an extension of breeding techniques, EPA determined that an adjective was needed to modify the word ''breeding'' to adequately describe the exempt group. Although the Agency used the word ''traditional'' in its 1994 proposed rule, EPA chose the word ''conventional'' to describe this type of breeding in this rule because the SAP/BSAC in their report of the January 21, 1994, joint meeting used the adjective ''conventional'' in its advice to EPA (Ref. 15), and the word ''conventional'' might more readily connote techniques such as wide crosses.

b. *Why is conventional breeding described by processes such as pollination and vegetative reproduction?* One comment received on the 1994 proposed rule suggested that there is ambiguity in the proposed regulatory language at 40 CFR 174.5(a) in the November 23, 1994, **Federal Register** document (59 FR 60535) about whether plant-incorporated protectants that are ''native'' to a food crop would meet the criteria of exemption.

Because of the use of the word ''food'' in the comment, it was not clear whether the comment is directed toward EPA's proposed exemption under FIFRA or that under FFDCA for residues of plant-incorporated protectants derived from sexually compatible plants. EPA assumes this comment is directed at both exemptions, and that the commenter's suggestion is that EPA ensure that the regulatory language exempts from FIFRA requirements, those plant-incorporated protectants that normally occur in a plant (i.e., are ''native'' to the plant) and will be used in that plant. For example, if corn normally produced a plant-incorporated protectant, the regulatory text should be clear that the plant-incorporated protectant would be exempt when produced and used in corn. EPA believes inclusion of the word ''pollination'' as an example of a process leading to syngamy in the definition of conventional breeding addresses this concern. Pollination, the transfer of pollen from an anther to a stigma (Ref. 9), is the process through which traditional breeding with most angiosperms, i.e., most major crop plants, occurs (see e.g., 59 FR 60537) (Ref. 9). Inclusion of the word ''pollination'' in the definition emphasizes that plant-incorporated protectants that occur naturally in a plant growing from a viable zygote that arises by the mating in conventional breeding of one corn variety with another, or the mating of a corn plant with a corn plant of the same variety are exempt.

EPA recognizes that this same concern of ambiguity also applies to plant-incorporated protectants in plants that are propagated vegetatively. EPA believes inclusion of the phrase ''vegetative reproduction'' in the definition of conventional breeding addresses this concern. The language of the exemption for plant-incorporated protectants derived through conventional breeding from plants sexually compatible with the recipient plant specifically exempts plant-incorporated protectants in plants reproduced vegetatively. For example, plant-incorporated protectants in a plant propagated only vegetatively, (e.g., bananas), are exempt. Also exempt are plant-incorporated protectants in a plant propagated primarily vegetatively (e.g., potatoes), as long as, under conditions of reproduction through hybridization, the plant donating the genetic material is sexually compatible with the recipient plant as defined in at 40 CFR 174.3, and the other conditions described at subpart B, in particular 40 CFR 174.25, are met. Inclusion of the term vegetative reproduction in the definition of conventional breeding reflects EPA's statement in the 1994 proposed rule (59 FR 60524) on the status of crop plant varieties propagated vegetatively.

c. *Will wide and bridging crosses be part of the definition of conventional breeding?* In this final rule, EPA is implementing a definition of ''sexually compatible'' that includes wide and bridging crosses. In this final rule, wide crosses means 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-pollination and post-pollination hormone treatments, manipulation of chromosome numbers, embryo culture or ovary and ovule cultures.

Generations of artificial hybridizations through these techniques have taken place in the well-established practices of plant breeding (Ref. 7). Wide crosses have been in the past, and are currently, commonly used to expand the plant gene pool for varietal improvement (Ref. 7), and a history of safe use has been associated with plant varieties developed through the use of wide cross techniques (Ref. 7). A fairly high degree of relatedness between the parental plants is indicated when a wide cross produces a viable zygote. This high degree of relatedness indicates a low probability of new exposures.

The definition of ''bridging crosses between plants'' is intended to convey the concept that an intermediate plant could be used in a cross to move traits from a source plant into a desired recipient plant. The intermediate plant can form viable zygotes with both the source and recipient plants, whereas the source and recipient plant cannot form viable zygotes. The intermediate plant serves as a bridge for gene flow between the two incompatible plants. 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. No comments were received on the proposed definition of bridging crosses between plants, also part of the definition of conventional breeding for sexually compatible. EPA is adopting this definition as proposed.

d. *Will cell or protoplast fusion be part of the definition of wide crosses?* EPA received one comment suggesting that protoplast fusion should be included in the definition of wide crosses between plants. In the technique of protoplast fusion, protoplasts are 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 are made from the somatic tissue of two different plants. The membranes of the different protoplasts are then fused together mechanically through processes such as treatment with polyethylene glycol, producing a hybrid somatic cell with a genetic make-up resulting from the combination and sorting of the two plant genomes. The somatic hybrid cell is then grown on specialized media into a mature plant.

In support of the request, the commenter argued that the hybridization of somatic cells has a history of use to artificially induce sexual compatibility. The commenter argued that movement of genetic material by this means has historically been considered safe.

EPA did not, in its 1994 proposed rule include protoplast fusion in the definition of wide crosses between plants, nor did it perform an analysis of the potential for new exposures when protoplast fusion is used to perform wide crosses between plants. The commenter did not provide such information in response to the 1994 proposed rule nor the 1997 supplemental document. EPA does not believe information currently in the record supports inclusion of protoplast fusion in the definition of wide crosses. Therefore, EPA does not in this rule include protoplast fusion in the definition of wide crosses, and specifically excludes cell fusion from the definition of conventional breeding. However, EPA requests comment on whether protoplast fusion should be included in the definition of wide crosses in a supplemental document published elsewhere in this issue of the **Federal Register**. EPA would welcome submission of information on protoplast fusion. If the Agency obtains sufficient information demonstrating a low probability of risk, EPA may initiate notice-and-comment rulemaking under FIFRA section 25(b) and FFDCA section 408 to include protoplast fusion in the definition of wide crosses between plants.

e. *''Recombinant DNA'' and genetic material ''extracted from an organism and introduced into the genome of the recipient plant.''* As explained previously, EPA restricted this exemption to conventionally bred plant-incorporated protectants while the Agency solicits additional comment on the alternatives it is considering in response to the comments received on the 1994 proposal. Thus, in order to fully describe which plant-incorporated protectants are exempt under this exemption, EPA includes limiting phases. EPA in the 1994 **Federal Register** document (59 FR 60529) discussion of the advice of the SAP and BSAC at the January 21, 1994 meeting on the use of a process-based criterion to define a category of plant-incorporated protectants that would be subject to review, stated that the Agency would define such a process-based criterion in the following way: ''The genetic material that encodes for the pesticidal substance or leads to the production of the pesticidal substance is extracted from an organism and introduced into the genome of the recipient plant or is synthesized *in vitro* and introduced into the genome of the recipient plant.'' In this action, EPA uses the language it put forth in the 1994 **Federal Register** document (59 FR 60529) to fashion two of the exclusions from the conventional breeding definition at 40 CFR 174.3. One exclusion is for techniques involving genetic material that has been extracted from the source and introduced into a recipient plant. Processes such as micro-injection, macro-injection and micro-encapsulation would be excluded from the conventional breeding exemption because they are used to introduce such extracted genetic material into the recipient plant. These processes have been included in the definition as examples to assist in understanding the concept.

The second exclusion from the conventional breeding exemption uses the term ''recombinant DNA'' to represent the concept of ''extracted from an organism. . ., synthesized *in vitro* and introduced into the genome of the recipient plant.'' To provide greater technical accuracy, EPA provides a definition at 40 CFR 174.3 for recombinant DNA as follows:

Recombinant DNA means the genetic material has been manipulated *in vitro* through the use of restriction endonucleases and/or other enzymes that aid in modifying genetic material, and subsequently introduced into the genome of the plant.

ii. *Why is the concept of ''functionally modified from the source'' important and how does the definition of conventional breeding address it?* In the November 23,1994 **Federal Register** document (59 FR 60524), EPA explained that in proposing the exemptions the Agency did not intend to exempt a plant-incorporated protectant that is significantly different in structure or function from a plant-incorporated protectant as it occurs in the source. EPA believed this limitation was appropriate because rearrangements or modifications of the genetic sequence encoding a pesticidal substance made through the use of techniques such as rDNA could, for example, result in a plant-incorporated protectant with significantly different functions from the functions 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. 7 and 16). Such a significantly modified plant-incorporated protectant 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. 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.

In this final rule, this concern is addressed by the limitation placed on the definition of sexually compatible. Under this definition, plant-incorporated protectants derived from plants sexually compatible with the recipient plant are only exempt if they are introduced into the plant through conventional breeding as defined at 40 CFR 174.3. The types of changes discussed above (Refs. 7 and 16) that can be made through modern molecular techniques, are very unlikely to be made through conventional breeding as defined at § 174.3, and plant-incorporated protectants modified through modern molecular techniques are not eligible for this exemption.

iii. *Why is the phrase ''never derived from source not sexually compatible with recipient plant'' important?* EPA discussed the relevance of this phrase to the exemption in the November 23, 1994 **Federal Register** document (59 FR 60523). The phrase, ''has never been derived from a source that is not sexually compatible with the recipient plant,'' which is part of the language of the exemption at 40 CFR 174.25, was meant to clearly indicate that a plant-incorporated protectant would not qualify for the exemption if the genetic material introduced into a recipient plant is from a sexually incompatible source and then this recipient plant subsequently used to move the introduced genetic material into plants sexually compatible with this first recipient plant. For example, the exemption does not extend to a situation where the genetic material encoding the *Bacillus thuringiensis* delta endotoxin is introduced into wheat, and the endotoxin-producing wheat is subsequently hybridized with rye using wide cross techniques to produce triticale. The endotoxin produced in the triticale would not be eligible for the exemption because the genetic material encoding the endotoxin originated from a bacterium, a source that is not sexually compatible with the original recipient plant (wheat in this example).

EPA received a comment that suggested that the Agency delete this phrase from the regulatory text and instead include a period of time after which a plant-incorporated protectant would be treated as part of a plant's ''accessible'' gene pool. EPA does not accept the suggestion to delete this phrase from the regulatory text, and continues to include this language in the final rule at 40 CFR 174.25. EPA will not implement the commenter's suggestion that a gene, derived from a phylogenetically distant source and successfully used in a crop, be treated after a period of time as though it had become part of the crop's gene pool (i.e., equivalent to a gene that had evolved in a sexually compatible population of plants). The commenter does not suggest what an appropriate period of time would be, nor how this would correlate with the potential for new exposures or low probability of risk. Without additional information, it is difficult for EPA to make a finding that there is a low probability of risk, or to assess the likelihood of unreasonable adverse effects as required by FIFRA section 25(b).

iv. *What other general qualifications apply to exemptions and how do these qualifications apply to plant-incorporated protectants derived through conventional breeding from sexually compatible plants?* EPA at 40 CFR 174.21 lists general qualifications that must be met in order to qualify for an exemption from FIFRA requirements. These include qualifications relating to plant-incorporated protectants intended to be produced and used in a crop to be used as food, and to inert ingredients.

a. *Plant-incorporated protectants in a crop used as food.* As noted in Unit II., the FQPA in 1996 modified the FIFRA definition of ''unreasonable adverse effects on the environment'' by adding a criterion requiring consistency with the standard under FFDCA section 408 (Public Law 104–170 (August 3, 1996)). EPA includes at 40 CFR 174.21 a general qualification that clearly states this requirement in the context of conditions necessary for the exemption of plant-incorporated protectants.

To understand how the status of a plant-incorporated protectant under FFDCA affects the status of the plant-incorporated protectant under FIFRA, the following must be considered: first, is the plant-incorporated protectant in a crop used as food; second, are the residues of the pesticidal substance and the residues of the genetic material of that plant-incorporated protectant exempt from FFDCA section 408?

Is the plant-incorporated protectant in a crop used as food? In order to exempt a plant-incorporated protectant from regulation under FIFRA, EPA must determine that the plant-incorporated protectant poses a low probability of risk, and will not cause unreasonable adverse effects on the environment even in the absence of regulatory oversight. How a plant-incorporated protectant can meet these standards differs somewhat depending on whether or not residues of the plant-incorporated protectant are in food. As noted in Unit II., as a practical matter a plant-incorporated protectant in 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 food.

If a plant-incorporated protectant is used in a crop used for food, unless there will be no residues in the food, the FFDCA section 408 requirements must be considered when determining whether the plant-incorporated protectant can be exempted from FIFRA requirements. To be exempted from FIFRA requirements, exemptions from the FFDCA requirement of a tolerance must exist for all of the residues of the plant-incorporated protectant. In accordance with the statutory definition of a ''pesticide chemical residue,'' EPA anticipates that in most cases the residues of a plant-incorporated protectant will consist of the pesticidal substance, the genetic material necessary to produce the pesticidal substance, any substance that might function as an inert ingredient as defined for plant-incorporated protectants (e.g., selectable marker), and the genetic material necessary for production of the inert ingredient (21 U.S.C. 321(q)).

If a plant-incorporated protectant is not used in a crop used for food (e.g., the plant-incorporated protectant is produced and used in a plant in a species used only for ornamental purposes), the FFDCA section 408 requirements do not need to be considered when determining whether the plant-incorporated protectant can be exempted from FIFRA requirements.

If the plant-incorporated protectant is used in a crop used as food, are the residues of the pesticidal substance exempt from FFDCA section 408? In a companion document published elsewhere in this issue of the **Federal Register**, EPA exempts from the requirement of a tolerance residues of the pesticidal substance portion of plant-incorporated protectants produced through conventional breeding from sexually compatible plants, and the residues of any substance used to confirm or ensure the presence of the active ingredient. The basis for this exemption is the determination that there is a reasonable certainty that no

harm will result from aggregate exposure to these residues. Thus, the answer to this question is yes for plant-incorporated protectants derived through conventional breeding from sexually compatible plants, with the limitation that the exemption does not apply when the residues are present in food at levels that are injurious or deleterious to human health. (For a detailed discussion of this limitation, see the companion document published elsewhere in this issue of the **Federal Register**.)

If the plant-incorporated protectant is used in a crop used as food, are the residues of nucleic acids that are part of a plant-incorporated protectant exempt from FFDCA section 408? The answer to this question is yes. In a companion document published elsewhere in this issue of the **Federal Register**, EPA exempts from the requirement of a tolerance residues of nucleic acids that are part of a plant-incorporated protectant because there is a reasonable certainty that no harm will result from aggregate exposure to these residues.

What is the status under FIFRA of plant-incorporated protectants derived through conventional breeding from sexually compatible plants in light of FFDCA requirements? Because of actions EPA takes in this document, and in two companion documents published elsewhere in this issue of the **Federal Register** under FFDCA section 408, plant-incorporated protectants derived through conventional breeding from plants sexually compatible with the recipient plant are exempt, whether or not they are in food, from all FIFRA requirements, except for the reporting requirements at 40 CFR 174.71.

b. *Inert ingredients*. EPA also includes at 40 CFR 174.21 a general qualification that describes how inert ingredients relate to the exemptions at 40 CFR part 174, subpart B.

With regard to how this general qualification applies to the exemption of plant-incorporated protectants derived through conventional breeding from sexually compatible plants, the preamble discussion in the 1994 **Federal Register** document (59 FR 60523) of the rationale supporting the proposal to exempt these plant-incorporated protectants extends to any substance that is derived from plants sexually compatible with the recipient plant, including substances such as a selectable marker, used to confirm or ensure the presence of the active ingredient. EPA's analysis in Units VII.D.3. and VII.D.4., applies equally to all the substances that normally characterize a population of sexually compatible plants, including inert ingredients, as long as these are derived through conventional breeding from plants sexually compatible with the recipient plant, and have never been derived from a source that is not sexually compatible with the recipient plant. An example of such an inert ingredient in sexually compatible plant populations could be tightly linked traits such as unusual leaf pigmentation always found with a pest resistance trait.

EPA includes in this final rule language at 40 CFR part 174, subpart X, to ensure that readers understand that any inert ingredient, and the genetic material necessary to produce it, that occurs naturally in a plant or is introduced through conventional breeding, is exempt when used with a plant-incorporated protectant derived through conventional breeding from a plant sexually compatible with the recipient plant. EPA believes this interpretation is a logical implication of the preamble discussion in the 1994 proposed rule (59 FR 60538).

Because the Agency recognizes that a substance with potential for adverse effects (i.e., a toxicant) could theoretically be used as a selectable marker, or inert ingredient, EPA places the same limiting condition on residues of the inert substance in food as is placed on residues of the pesticidal substance portion of the active ingredient; i.e., the residues of the substance portion of a selectable marker, or inert ingredient, do not qualify for the exemption if they are present in food from the plant at levels that are injurious or deleterious to human health.

Additional findings and conclusions supporting this exemption may be found in the companion document published elsewhere in this issue of the**Federal Register** entitled ''Exemption from the Requirement of a Tolerance under the Federal Food, Drug, and Cosmetic Act for Residues Derived Through Conventional Breeding from Sexually Compatible Plants of Plant-Incorporated Protectants.''

The regulatory text of new 40 CFR 174.485, which is entitled ''Inert ingredients from sexually compatible plant,'' can be found in the regulatory text of this document.

Under section 408(g) of the FFDCA, as amended by the Food Quality Protection Act (FQPA), any person may file an objection to any aspect of this subpart X regulation and may also request a hearing on those objections. The EPA procedural regulations which govern the submission of objections and requests for hearings appear in 40 CFR part 178. Although the procedures in those regulations require some modification to reflect the amendments made to the FFDCA by the FQPA. EPA will continue to use those procedures, with appropriate adjustments, until the necessary modifications can be made. The new section 408(e) provides essentially the same process for persons to ''object'' to a regulation for an exemption from the requirement of a tolerance issued by EPA under new section 408(e), as was provided in the old FFDCA sections 408 and 409. However, the period for filing objections is now 60 days, rather than 30 days. For more details on filing objections or requesting hearings pursuant to regulations promulgated under the FFDCA, see the discussion in the companion document published elsewhere in this issue of the **Federal Register** (under ''Objections and Hearing Requests'').

v. *What were the other potential approaches to scope of exemption?* In the November 23, 1994 **Federal Register** document (59 FR 60523), EPA discussed the merits of two approaches using taxonomy, in whole (Option 2) or in part (Option 3), as a standard for describing closely related plants, and received comment on use of such a criterion. EPA also received a comment suggesting that the criterion of sequence homology be used to limit the concept of sexual compatibility.

a. *Taxonomy*. Two commenters expressed reservation about using a taxonomic standard for describing closely related plants. They pointed out that taxonomic categories, and the relationship of a given plant species to a given taxon, may be transient since taxonomic classification may change as information accrues. EPA noted in the discussion of Option 2 and Option 3 in the 1994 **Federal Register** document (59 FR 60524) that a taxonomy-based standard may be artificial: classification of plants in different taxonomic genera is not fixed and could change over time and between scientific authorities. Taxonomy reflects current observations about phenotypic, and to some extent, genotypic, differences between organisms. Currently, some plant genera are narrowly defined; for other plant genera, membership is based on broader criteria. These differences in classification criteria may lead to different probabilities between genera that new exposures may occur when genetic material from one species in a genus is introduced into another species in the genus. In recent years new tools have become available to taxonomists, allowing them to better clarify phylogenetic relationships among organisms. New information,

particularly that obtained through the use of new genetic tools, concerning organisms' properties and relationships may in the future alter current taxonomic designations. In light of these advances, EPA anticipates there may be some reorganizations among the Plantae, and that these reclassifications will better reflect the relationships among plants, and the probability of new exposures in intrageneric crosses.

The possibility that taxonomic classification may change as information accrues adds an extra layer of complexity to any regulations based on a taxonomic standard, and EPA probably would not be able to structure an exemption to accommodate for potential changes in classification. The possibility of reclassification also creates some uncertainty within the regulated community about the future status of a product.

In addition, taxonomy may be a more artificial standard than sexual compatibility as a predictor of different environmental exposures of a plant-incorporated protectant, particularly for unmanaged or semi-managed plants. Isolation, adaptation to unique environments, and low natural rates of gene flow characterize many natural populations. For these types of plants, a taxonomic standard may not be as appropriate as a standard based on sexual compatibility with regard to novel exposures to plant-incorporated protectants. At the January 21, 1994, joint meeting of the Subpanel of the SAP and the BSAC Subcommittee, the scientific advisory groups questioned whether the reasoning supporting use of a standard based on sexual compatibility supported equally well a standard based on taxonomy for semi-managed plants (e.g., trees). They indicated it probably did not for the reasons cited in this paragraph (Ref. 15).

b. *Sequence homology*. The suggested criterion of sequence homology would base relatedness on the degree of sequence homology between the source and recipient plant. Sequence homology refers to the extent that the sequence of deoxynucleotides in two pieces of genetic material are the same (Ref. 17). A deoxynucleotide is made up of a sugar, a phosphate, and one of four purine or pyrimidine bases (adenine, cytosine, guanine, thymine). The sugars and phosphates of the deoxynucleotides are covalently linked by phosphodiester bonds to form the ''backbone'' of the deoxynucleotide polymer (DNA). One base is attached to each sugar in the sugar-phosphate backbone. The information encoded in the genetic material is determined by the sequence in which the bases are attached to the sugar-phosphate backbone. The extent to which two pieces of genetic material have the same base sequence is often described in terms of percent homology, with 100% homology meaning the pieces of genetic material have an identical sequence. The Agency believes that, in general, DNA sequence homology is a less straight-forward standard for regulatory purposes than a standard such as sexual compatibility. Sexual compatibility is known in most cases, and if it is not, it is less burdensome and simpler to demonstrate than is relatedness based on DNA sequence homology. Use of homology as a criterion presents the following complex issues. First, where should homology be assessed? For example, how many genes of the source and recipient plants should be compared to determine the degree of homology? All the genes of both plants? A few genes? If only a few, which genes? Second, what degree of homology would be sufficient to indicate a high degree of relatedness? Third, under what conditions should homology be measured? Fourth, appropriate test procedures would need to be developed and validated in order to set a standard procedure for measuring homology. All of these issues would need to be resolved, and converted into regulatory text, in order to develop an exemption standard based on DNA sequence homology.

2. *How did EPA assess this category of plant-incorporated protectants?* Typically, in assessing a pesticide for environmental risk, EPA uses the information requirements generated pursuant to 40 CFR part 158 to evaluate the potential effect of the pesticide on birds, mammals, freshwater fish and invertebrates, estuarine and marine animals, and nontarget plants and insects (e.g., predators, parasites and honey bees). For most pesticides, this information is generated using animal models. To address these same questions for the plant-incorporated protectants that are the subject of this exemption, EPA was able to rely on the large and varied information base available in the public scientific literature.

Generally, when EPA assesses the risks caused by the use of a pesticide, it considers both the potential hazard that the pesticide poses to the environment and the potential for exposure to the pesticide due to its use. For most pesticides (e.g., chemical pesticides), EPA's risk evaluation relies on data generated by testing in laboratories using representative animal models to estimate risk end-points. Other information, including product analysis data and information generated by use of mathematical models, are used to develop exposure estimates. Exposure and hazard estimates are combined to quantify the potential risk associated with the pesticide's use. The data requirements describing the types of information to be generated and other guidance for assessing risk is detailed in 40 CFR part 158.

The questions posed as part of the risk assessment in evaluating most pesticides (e.g., chemical pesticides) can also be posed for the plant-incorporated protectants that are exempted in today's action, and 40 CFR part 158 can be used as guidance. EPA adopted an approach for evaluating the potential risks of plant-incorporated protectants exempted by this final rule, that is consistent with the unique characteristics of pesticides produced and used in a living plant, and the scientific knowledge and experience accumulated on these substances.

To address the hazard endpoints described in 40 CFR part 158 for the plant-incorporated protectants that are the subject of this exemption, EPA relied on a very large body of information developed through systematic scientific study that exists in the public literature (Ref. 18). This literature was developed through many decades of testing and observation. EPA thus could rely on this information and did not need to rely only on animal model testing to assess risk. EPA was also able to rely on information in the literature in evaluating the potential for exposure to the plant-incorporated protectants that are the subject of this exemption. Plant-incorporated protectants are produced within the living plant and the pesticidal substance is used *in situ* in the plant and this affects the exposure paradigm.

3. *On what basis did EPA determine that plant-incorporated protectants derived through conventional breeding from sexually compatible plants present a low probability of risk?* EPA considered several factors in determining whether plant-incorporated protectants derived through conventional breeding from sexually compatible plants could be exempted from FIFRA requirements. These include: First, the large body of knowledge that currently exists on plants in sexually compatible populations derived through conventional breeding; second, the potential for novel exposures; third, the potential for quantitative changes in the levels of substances normally found in plants in sexually compatible populations that might cause adverse effects; and, fourth outcrossing of the

ability to produce these substances to wild or weedy relatives. To support its conclusions that this category of plant-incorporated protectants present a low probability of risk, EPA also relied on the analyses laid out in the tolerance exemptions published elsewhere in companion documents in this issue of the **Federal Register**. Rather than reiterate all of these analyses here, EPA refers readers to the detailed discussions in those documents. EPA believes that the conclusions reached for plant-incorporated protectants derived through conventional breeding from sexually compatible plants also apply for other substances that might be considered part of the pesticide product (e.g., inert ingredients) for these plant-incorporated protectants.

i. *Large body of knowledge and experience exists.* In the issue paper entitled ''FIFRA: Benefit and Environmental Risk Considerations for Inherent Plant-Pesticides,'' (Ref. 18) EPA describes a large part of the information base on nontarget plants, insects, birds, mammals and other herbivores the Agency utilizes for its evaluation of the potential effects of the plant-incorporated protectants that are the subject of this exemption (Ref. 18). In addition, EPA uses the large literature on the effect on humans of consumption of food from plants in sexually compatible populations developed through conventional breeding generated from epidemiological studies, nutritional assessments, animal model testing and biochemical studies (Refs. 7, 8, 19, 20, 21, 22, 23, 24, 25, 26, and 27) to draw conclusions on the potential risk for animal non-targets, including birds and fish, which might consume food or feed containing plant-incorporated protectants that are the subject of this exemption. Just as testing in animal models can supply information that is extrapolated to conclusions on the effect of a substance on humans, so too can information and conclusions drawn in the dietary risk assessment on the effects on humans be extrapolated to predict effects on non-human mammals and other animals in an assessment of environmental risk. In addition, there is a long history of hundreds, if not thousands of years, of humans using foods containing the plant-incorporated protectants that are the subject of this exemption as feed for domesticated and other animals, including birds and fish (Ref. 28, for example). EPA relies on these experiences and the large literature generated by a century of systematic studies of the constituents of food (Refs. 7, 8, and 18) to assess the plant-incorporated protectants that are the subject of this exemption.

EPA also took into account scientific knowledge from a number of disciplines including plant genetics, plant physiology, phytopathology, entomology, biochemistry, microbial ecology, ecology and plant breeding. From these disciplines, EPA considered, for example, information on plant metabolism, the production of substances that may have a pesticidal effect, and conditions that may limit the production of such substances (Refs. 9, 17, 18, 29, and 30). The Agency also used experimental data derived from the science of phytopathology to characterize the pest resistance mechanisms in plants (Ref. 29).

ii. *Low potential for novel exposures.* Humans and the environment are currently being, and have been for long periods of time, exposed to plants containing the plant-incorporated protectants that are the subject of this exemption. Based on the knowledge base described above in Unit VII.D.2., current conditions of exposure pose a low probability of risk.

Sexually compatible plants share a common pool of genetic material, even though there may be some variability among plants in sexually compatible populations. Sexual compatibility, the ability to produce viable offspring, is only possible in nature for organisms that possess many traits in common. Traits, and the genetic material encoding them, can be passed through a sexually compatible plant population by mating, and the mixing of genetic material that occurs through mating tends to a situation where the members of a sexually compatible population have similar traits and similar genetic material. Thus, movement through conventional breeding of genetic material encoding pesticidal substances between plants in a sexually compatible population is unlikely to result in exposure of organisms that associate with a plant in that population to plant-incorporated protectants that they, and their ancestors, had not been exposed to previously. If a population of plants normally possesses a pesticidal substance, organisms that come into contact with some plants in that population have likely been exposed to that substance in the past, perhaps over long periods of time. These past exposures, particularly if they occur over long periods of time, may lead to a degree of adaptation, or tolerance, in the population of organisms exposed to the pesticidal substance (Ref. 9). The potential for novel, or significantly different environmental exposures to occur in such a situation, would be low.

Further, the potential for exposure to plant-incorporated protectants is in general lower than for other types of pesticides, because plant-incorporated protectants are produced within the living plant and used *in situ* in the plant. Most other pesticides must be applied to the plant, or near the plant. Because a plant-incorporated protectant is produced and used within the plant, physiological constraints limit the amount of pesticidal substance produced by the plant. Because the plant-incorporated protectant is within the plant, the routes by which other organisms may be exposed to the plant-incorporated protectant may be more limited, e.g., dietary exposure is likely to be the predominant route of exposure. Because plant-incorporated protectants are produced and used in the living plant, actual physical contact with the plant or plant parts will, in general, be necessary for exposure to occur. In addition, the plant-incorporated protectants exempted by this final rule are part of the metabolic cycles of plants. They, thus, are biotic and are subject to the processes of biodegradation and decay that all biotic materials undergo (Ref. 31). Biotic materials are broken down to constituent parts through the enzymatic processes of living organisms, and these constituent parts used as building blocks to make other biotic substances. Furthermore, the plant-incorporated protectants that are exempted in this action are biodegradable to their constituent elements through catabolism by living organisms. Because of their biodegradable nature, these plant-incorporated protectants do not bioaccumulate (bioaccumulation occurs when a substance is taken into the body through processes such as eating, and as the body is unable to either break the substance down or eliminate it, the substance accumulates in the tissues) or biomagnify (biomagnification occurs when a substance bioaccumulates in the bodies of organisms lower in the food chain, and as predators higher in the food chain consume organisms lower in the food chain, more and more of the substance accumulates in the bodies of organisms higher in the food chain) in the tissues of living organisms as do substances, such as dioxin (Ref. 32). Because of these characteristics, the potential for new exposures to occur, beyond direct physical exposures to the plant or plant parts, is limited for plant-incorporated protectants derived through conventional breeding from sexually compatible plants.

EPA received a comment raising the concern that ''wild-type or

conventionally bred plants in new environments attract, repel or otherwise influence biota surrounding them.'' In response, EPA would first point out that as described in Unit VII.B.5., a key statutory element in the FIFRA definition of pesticide is whether a human ''intends'' that a substance or mixture of substances be used for destroying, preventing, repelling or mitigating a pest. A plant introduced into the United States with reference only to its ornamental beauty or its food value, without regard to ability to resist pests, does not contain substance(s) meeting the FIFRA section 2(u) definition of pesticide until a human intends the substance(s) be used for preventing, destroying, repelling or mitigating a pest. Substances within a plant introduced into the United States with pesticidal claims are pesticides within the FIFRA section 2(u) definition. However, as pointed out by the commenter, these substances would be exempt from FIFRA requirements if derived through conventional breeding from sexually compatible plants even though they present a potential for novel environmental exposure. EPA believes this is appropriate. When EPA proposed to exempt plant-incorporated protectants derived from sexually compatible plants from FIFRA requirements, EPA recognized that most crop plants, including all major crop plants, were not native to the United States. The risk assessment the Agency performed and its analysis of risks versus benefits as prescribed by FIFRA, led it to propose the exemption based on a determination that the benefits of use of agricultural crops already in the United States outweigh the low probability of risk. The Agency also anticipated that the probability that nonindigenous plants representing wide-spread exposure being commercially introduced into the United States with pesticidal claims in the future was low (Ref. 7). EPA also considered that the adverse effects reporting requirement it was placing on the exemption would serve to alert the Agency should any environmental or human health risk be identified with such plants. In addition, EPA considered whether new dietary exposures could occur with such plants. EPA concluded that for any such plant introduced into the United States for food use, there will likely be in the country of origin, a history of experience with the dietary use of the plant or parts of the plant, even if a similar history does not exist in the United States at the time of the introduction. In performing its analysis of dietary risk, EPA found no basis for assuming that the dietary effects of any plant-incorporated protectant residues in such a food from such a plant would differ for the United States population from that of the source country. Moreover, EPA believes that the limitation in the tolerance exemption for residues of the pesticidal substance portion of plant-incorporated protectants derived through conventional breeding from plants sexually compatible with the recipient plant will allow EPA and FDA to act expeditiously should any substances meeting the FIFRA section 2 definition of pesticide be identified as problematic.

iii. *Low potential for significant increases in levels of plant-incorporated protectants.* EPA has evaluated whether there are likely to be quantitative changes in levels of plant-incorporated protectants derived through conventional breeding from sexually compatible plants, such that adverse effects on the environment might occur. EPA has determined that the probability of such an event is low because the highest levels of pesticidal substances likely to be attained with plant-incorporated protectants in this group are not likely to result overall in significantly different environmental exposure levels. This analysis was presented in an EPA issue paper, entitled: ''Benefit and Environmental Risk Considerations for Inherent Plant-Pesticides'' (Ref. 18) located in the record for this rule as described in Unit VIII. A summary of the analysis is presented here.

EPA first considered whether an increase in the levels of substances, including plant-incorporated protectants, that plants normally produce is likely to exceed the ranges normally found within and between plant varieties and uncultivated plants. The level of production of such substances normally varies among sexually compatible plants because of differences in potential to express a substance and environmental conditions. Indeed, variation is seen even among plants in the same variety because of differences such as weather and soil condition. For example, one report (Ref. 7) has shown an 8.3-fold variation in the amount of ascorbic acid in turnip greens depending on the degree of exposure to light. Such variation could also characterize natural variation in the levels of a plant-incorporated protectant and variation in exposure for organisms that associate with the plant. Nontarget organisms, such as birds and insect pollinators, that associate with plants have been, and are currently being exposed to the range of levels of plant-incorporated protectants being expressed by plants within sexually compatible populations. This exemption will not affect these exposure patterns.

EPA also considered the extent to which any substance can be increased in highly managed plants without unwanted effects on other, desirable characteristics of the plant such as yield or palatability of fruit. In general, breeders balance all of these characteristics in developing marketable plant varieties. Plants have, as do all organisms, only a limited capacity to express a particular trait without a drain on energy reserves. Greatly increased levels of a plant-incorporated protectant would, in general, only be accomplished at the expense of the expression of other, agriculturally desirable traits (Ref. 18).

EPA anticipates that for the majority of agricultural plants, levels of expression of substances such as plant-incorporated protectants will continue to fall within currently observed ranges of expression; EPA does not anticipate that variations in the level of a plant-incorporated protectant that is normally a component of a plant and derived through conventional breeding from plants sexually compatible with the recipient plant would lead to a significantly different spectrum of exposure to a plant-incorporated protectant. Moreover, EPA believes that the history of familiarity with agricultural plants in sexually compatible populations, and thus with the likely progeny of genetic exchanges between plants in such populations, and the procedures currently employed in plant breeding to screen out undesirable traits also support this conclusion.

Comments on quantitative changes and on the potential for plants consumed *in toto* or in part as food to produce injurious or deleterious effects have, however, caused EPA to reconsider its approach under FFDCA to pesticidal substances derived through conventional breeding from sexually compatible plants. To address concerns raised in comment on the possibility that certain substances normally present in plants in sexually compatible populations may in rare circumstances be present in food at levels that are hazardous, EPA places a condition on the exemption under FFDCA section 408 for pesticidal substances derived through conventional breeding from sexually compatible plants. Eligibility for exemption is based on the condition that the residues of the pesticidal substance not be present in food from the plant at levels that are injurious or

deleterious to human health. If the residues of the plant-incorporated protectant do not meet this criterion, they are not exempt from the requirement of a tolerance. Because the residues would not qualify for the exemption and no tolerance would have been established, any food containing such residues would be ''adulterated'' pursuant to section 402(a)(2)(A) of the FFDCA and subject to seizure (21 U.S.C. 342 (a)(2)(A)). As noted in Unit II., the status of a plant-incorporated protectant under FFDCA can affect its status under FIFRA.

EPA also considered issues of variation in levels of plant-incorporated protectants and exposure of nontarget organisms to such plant-incorporated protectants for plants in semi-managed systems (e.g., trees) (Ref. 18). EPA anticipates that for such plants, levels of expression of substances such as plant-incorporated protectants will continue to fall within currently observed ranges of expression. EPA does not anticipate that variations in the level of a plant-incorporated protectant in these plants would lead to a significantly different spectrum of exposure to a plant-incorporated protectant. It is not anticipated that the levels of plant-incorporated protectants in these plants would significantly exceed existing expression ranges of their free-living relatives (Ref. 18).

One commenter worried that because levels of substances in plants vary in response to environmental conditions, the legal status of a plant-incorporated protectant could change from exempt to non-exempt as the levels of pesticidal substances fluctuate. While it is possible, particularly in light of the condition placed on the exemption from the requirement of tolerance, that the legal status of a plant-incorporated protectant could change from exempt to non-exempt, EPA anticipates this will occur only very rarely, if at all. In its assessment, EPA considered the probability of variations in levels of plant-incorporated protectants derived through conventional breeding from sexually compatible plants presenting risk. EPA concluded that although variations will occur in response to environmental conditions, in the range of levels likely to occur they pose a low probability of risk from quantitatively different exposures. EPA's conclusion that it is unlikely that variation due to environmental conditions, or to breeding decisions, would result in risk from quantitatively different exposures is reflected in the Agency's reliance on the post marketing monitoring afforded by the adverse effects reporting requirement at 40 CFR 174.71.

iv. *Low potential for weediness from outcrossing from plants derived through conventional breeding to wild relatives.* A question directly affecting the exposure component of the risk assessment that has no equivalent in the assessment of more traditional pesticides (e.g., chemical pesticides) must be posed for plant-incorporated protectants. Because plant-incorporated protectants are produced and used in the living plant, the possibility that the ability to produce a plant-incorporated protectant may be transferred by outcrossing and hybridization from the crop plant to a cultivated, wild or weedy relative was considered for the plant-incorporated protectants exempted in this action. A large volume of information is available in the public literature (Ref. 33) on this possibility for plant-incorporated protectants derived through conventional breeding from sexually compatible plants. EPA's issue paper entitled ''Risk Considerations for Outcrossing and Hybridization'' describes in part the information base used to address this aspect of the assessment (Ref. 33).

One of the considerations evaluated for this exemption was whether a capacity to express higher levels of pesticidal substances could be transmitted to wild relatives through outcrossing of the genetic material necessary for the production of the pesticidal substance. A second and more important consideration is whether such an outcrossing event, could in turn, increase weediness of the wild relative. EPA believes that the potential for weediness to increase in wild relatives through the transfer of the genetic material for the pesticidal substance from a crop plant is low for the following reasons.

First, there are several factors which govern whether gene flow occurs between crops and their wild relatives (Ref. 34). Genetic barriers can prevent hybrids from forming, render them sterile, or reduce the fertility of hybrids, and, thus, restrict their contribution to subsequent generations. The strength of genetic barriers is correlated to degree of evolutionary relatedness between the crop and wild relatives (Ref. 34). Space is an effective barrier to hybridization. The wild relatives of corn with which it can hybridize, are restricted to Mexico and Central America. There is no danger of hybridization in other regions (Ref. 34). Time of flowering can prevent hybridization when there is no overlap in the time of flowering of cultivated and wild forms (Ref. 34). The breeding system of the crop plays an important role. For some species (e.g., peanut), the flowers do not ordinarily open, and self-pollination may be very near 100% (Ref. 34). The ploidy level may differ between a crop and its relatives, and differences in ploidy levels can severely reduce the likelihood that the cultivated plant and wild relative will form fertile hybrids (Ref. 34). Some varieties of certain crop species, such as banana, are sterile, and thus are incapable of hybridizing not only with members of other species, but also of their own species (Ref. 34). For some crops in the United States, the probability of gene transfer and hybridization with the wild relative is zero, while for other crops, despite the variety of potential barriers to and selection against hybridization, it is possible.

Second, in general, wild members of sexually compatible populations tend to already possess higher levels of resistance to pests and disease than do the cultivated members of those populations (Ref. 18). Wild members of sexually compatible plant populations also tend to express a greater range of levels of inherent plant defense compounds than do cultivated plants, including production of higher levels of substances that could potentially be used as plant-incorporated protectants (Ref. 18). Indeed, during the past 100 years, it has been common practice to cross crop plants with sexually compatible wild relatives, since these wild relatives usually have higher levels of resistance to a pest, in order to develop crop varieties with improved resistance to the pest. For example, wild species of tomatoes have been used, in conventional plant breeding, as a source of increased resistance to economically important diseases in tomato (Ref. 7).

EPA anticipates that for the majority of agricultural and semi-managed plants, levels of expression of substances such as plant-incorporated protectants, within plants in sexually compatible populations, will continue to fall within currently observed ranges of expression. EPA does not anticipate that variations in the levels of substances such as plant-incorporated protectants, that are normally components of a plant would lead to a significantly different range of expression as a result of this exemption (Ref. 18). Thus, even should a crop plant containing a plant-incorporated protectant in this exempt category hybridize with a wild relative, it is unlikely that the range of expression of the plant-incorporated protectant by the wild relative will be substantially increased by acquisition of the trait from the crop plant.

4. *On what basis did EPA determine that these plant-incorporated protectants are not likely to present*

unreasonable adverse effects to the environment even in the absence of oversight? As explained in Unit II., a pesticide chemical meets the standard for a FIFRA 25(b) exemption if the risks resulting from use of that pesticide are consistent with the FFDCA section 408 exemption standard, and the potential benefits of use outweigh any human health or environmental risks even in the absence of regulatory oversight. EPA considered several factors in determining whether the exempted plant-incorporated protectants are not likely to cause an unreasonable adverse effects to the environment. These include consideration of the potential for dietary, both non-occupational and occupational human health risks, and environmental risks. Also considered was whether the language of the exemption clearly describes for the regulated community what plant-incorporated protectants are exempt; how the scope of the exemption under FIFRA relates to a companion exemption from the FFDCA requirement of a tolerance for residues of these plant-incorporated protectants; and general benefits to society, growers, consumers and the environment.

Some of these considerations were analyzed in detail in the tolerance exemptions published elsewhere in companion documents in this issue of the **Federal Register**. Rather than reiterate the analyses here, the Agency has, in this section, limited its discussion of the human health risks addressed in great detail in those documents to the remaining risks for which the probability is so low that, notwithstanding their existance, the residues meet the section 408(c) standard. The standard for granting an exemption under section 408(c) requires a ''reasonable certainty of no harm,'' not absolute certainty. EPA can make the safety finding required under FFDCA section 408(c) based on an extremely low probability or risks; a demonstration of ''no risk'' is not required.

i. *Dietary risk considerations*. EPA has determined that there is a reasonable certainty that no harm will result from aggregate exposure to residues of the plant-incorporated protectants that are the subject of this exemption. For a full explanation of the factual bases for this determination, readers are referred to EPA's assessment of human dietary risks in the tolerance exemptions published elsewhere in companion documents in this **Federal Register**, and to related documents in the record for the rule as described at Unit VIII.

In addition, the Agency evaluated the remaining dietary risks that pose a negligible probability of causing adverse effects. As explained throughout this preamble, and in associated rules, EPA believes that the likelihood of dietary risks associated with the residues of plant- incorporated protectants that are the subject of this exemption are extremely low. However, it is possible that, notwithstanding the best efforts of plant breeders, a toxicant could enter the food supply at levels that could cause adverse effects. Because of the conditions of the exemption, such food would no longer qualify for the exemption, and would be subject to seizure. Thus, the extent of the harm is anticipated to be extremely low.

ii. *Occupational and non-occupational risk to humans*. Plant-incorporated protectants are likely to present a limited exposure to humans. In most cases, the predominant, if not the only, exposure route will be dietary. Significant respiratory and dermal exposures are unlikely because the substances are in the plant tissue and thus are found either within the plant or in close proximity to the plant. Although a potential for non-dietary exposure (e.g., dermal and inhalation) in occupational settings may exist, EPA expects such exposure to be negligible and thus human health risks to be negligible.

a. *Dermal exposure*. Plant-incorporated protectants derived through conventional breeding from sexually compatible plants may in some cases be present in sap or other exudates from the plant or the produce and thus may present some limited opportunity for dermal exposure to persons coming physically into contact with the plant or raw agricultural food from the plant. Farmers and food handlers (e.g., individuals harvesting produce by hand, preparing food for sale, or stocking produce bins in grocery stores) or floral workers, are those most likely to experience dermal contact with the substances on an occupational basis. Although contact dermatitis is fairly common in such workers (Refs. 35 and 36), these dermal reactions are generally mild, of a self-limiting nature or self-diagnosed, and treated.

Most of the substances that could be the subject of this exemption are unlikely to pass through the skin to affect other organ systems (Refs. 36 and 37). For those substances which possess to some degree properties that allow some penetration of the skin, the potential amounts passing through the upper layer of the skin (epidermis) are negligible or the substances do not present adverse effects (Ref. 36).

A group of substances that might be plant-incorporated protectants, if humans intend to use them as pesticides, with the ability to present an effect on dermal exposure in the occupational setting beyond a mild contact dermatitis are the psoralens. These substances occur naturally in a wide range of plants but occur in the highest concentrations in celery, dill and parsley (Refs. 8 and 36). Psoralens can be phototoxic to the skin in conjunction with sunlight (UV light). Due to their relative solubility in oils, psoralens can penetrate into the skin cells, where they intercalate into the genetic material of the skin cell (Ref. 8). Subsequent exposure to sunlight (UV light) causes the genetic material to ''cross link'', affecting the ability of the cell to further process its genetic material. This may result in skin blisters and rashes. This UV-dependent phototoxicity has also been implicated in mutations that may lead to skin cancer (Ref. 8). In spite of the potential for this type of adverse effect with the psoralens, there are few reported incidents of this type of problem for substances derived through conventional breeding from sexually compatible plants. There is one reported incident in the 1980's where a celery variety with high levels of psoralen caused rashes and dermatitis in produce handlers (Ref. 7). The problem was identified and the variety removed from the market.

b. *Inhalation exposure*. Plant-incorporated protectants derived through conventional breeding from sexually compatible plants may in some cases be present in pollen and some individuals (e.g., those working on farms in nurseries or other plant-growing areas) may be exposed, through inhalation, to wind-blown pollen. When present in pollen, the pesticidal substance is likely to be integrated into the tissue of the pollen grain. Pollen grains are solid, insoluble particles of sufficiently large diameter that they are filtered out in the nasopharynx or in the upper respiratory tract (Refs. 36 and 38). This exemption will not change current exposures nor affect strategies for dealing with plant-incorporated protectants that are the subject of the exemption (Refs. 36 and 38).

iii. *Environmental considerations*. EPA examined, in Unit VII.D.3., the potential for environmental effects from the plant-incorporated protectants that are exempted by this action. The Agency has determined on the basis of its analysis that the probability of novel exposures to nontarget organisms and to the surrounding ecosystems are low. EPA's analyses indicate that the risks of outcrossing with wild relatives are also anticipated to be low. Similarly, EPA's

analyses indicate that the risks of groundwater, or surface water, contamination from these products are extremely low. EPA has thus concluded that potential risks of environmental effects are not significant.

iv. *Exemption criteria provide high degree of regulatory clarity.* EPA believes that using sexual compatibility coupled with the process by which the plant-incorporated protectant is introduced into a plant as a standard affords the most clear description of whether a plant-incorporated protectant is exempt. Most plants have some form of sexual reproduction characterized by the formation of gametes from haploid germ cells, although some do not (Ref. 9). The definition of conventional breeding at 40 CFR 174.3 provides for this latter category of plants, which reproduce vegetatively. Plants reproduce either by sexual processes or vegetative reproduction, and the limitations posed by these natural barriers limits the transfer of genetic material to plants within a sexually compatible population. These barriers can also be effectively used to establish scope within regulations for plants.

In most cases, whether two plants are sexually compatible is known; thus, testing to determine whether the plants are sexually compatible is not likely to be necessary. If, in some cases, it is not known whether two plants are sexually compatible, the means of determining sexual compatibility is straightforward and simple. Sexual compatibility is empirically demonstrable. EPA believes that a standard based on sexual compatibility provides a high level of regulatory clarity and great ease of implementation. This standard allows the public, industry, and EPA to easily and readily identify those plant-incorporated protectants that are exempt.

v. *Exemption criteria create similar scopes under FIFRA and FFDCA section 408.* When EPA proposed its exemptions in 1994, one of its goals was to create as similar a scope of exemption under FIFRA and the section of FFDCA dealing with pesticides as possible, given the differences in mandate and structure of the two statutes. EPA believed that because it utilized the two authorities in concert to regulate pesticides, similar exemptions under the two statutes would be desirable. Such an approach would be simpler for the regulated community to understand and for EPA to administer.

In considering dietary risk under FFDCA section 408, EPA concluded that a standard based on sexual compatibility exempts those plant-incorporated protectants for which there is a reasonable certainty that no harm will result from aggregate exposure. EPA, in a companion document published elsewhere in this issue of the **Federal Register**, exempts from the FFDCA section 408 requirement of a tolerance, residues of pesticidal substances derived through conventional breeding from sexually compatible plants. The information supporting that exemption was generated on food from plants in sexually compatible populations developed through conventional breeding.

vi. *No undue burden.* The standard provided by criteria based on sexual compatibility creates a similar exemption under FFDCA and FIFRA, while at the same time implementing the standard with a high degree of regulatory clarity. Implementing a standard with a high degree of regulatory clarity that also creates similar exemptions under FFDCA and FIFRA results in less burden on producers. In addition, EPA believes that implementation of the exemption described in this document, and the exemptions under FFDCA section 408 published elsewhere in companion documents in this issue of the **Federal Register**, and the clarification that plants used as biological control agents are exempt from FIFRA requirements, minimize the burden of producers/developers while appropriately addressing risk.

One comment questioned the cost of EPA's proposed exemptions (59 FR 60519), appearing to believe that research scientists and industry would have to notify and consult with EPA in order to qualify for exemption. This final rule does not require producers to notify or consult with EPA, or present data to the Agency in order to qualify for exemption. The producer would determine whether a particular plant-incorporated protectant meets the exemption criteria. EPA expects that a producer will not have to create additional information specifically to determine if a product is exempt, because producers will already have such information from the ordinary course of product development. There is no requirement to notify EPA associated with the exemption, and no costs can be ascribed to such a notification process.

Some comments offered general observations that costs would curb the development of crop varieties. EPA believes that the clarification that it will not regulate plants per se, and the exemptions it is publishing in this document and in companion documents in this issue of the **Federal Register**, limit EPA's effect on plant breeding and allow most aspects of plant breeding to be pursued without EPA regulation.

Some comments suggested that costs would inhibit the development of alternatives to chemical pesticides. EPA has been, and continues to be, committed to the development of safer pesticides, many of which are biological pesticides, as possible alternatives to more toxic pesticides. The Agency believes the actions it takes with regard to plant-incorporated protectants encourage public confidence in the safety of plants and foods from plants, developed using traditional and modern techniques of biotechnology. The Agency believes that consumer acceptance is key to the success of agricultural products, and that consumer acceptance is strongly influenced by confidence that regulatory agencies have ensured the public safety.

vii. *Benefits.* The benefits to society associated with exemption from FIFRA requirements of this category of plant-incorporated protectants include general benefits to society from the practices of horticulture and of agriculture in producing the food supply and other plant based products (e.g., fiber, lumber), and economic benefits to growers, and the environment.

a. *General benefits to society.* Agriculture based on conventional breeding allows much of the current world population of 6 billion humans to feed itself. Development of higher yielding varieties through conventional breeding in sexually compatible crop plant populations has been an important means of feeding a growing human population (Refs. 39 and 40). For example, it has been estimated that the development of new varieties of plants in sexually compatible populations through conventional breeding accounts for about 80% of the increase in corn yields from 1930 to 1980 and more than half of the increase in soybean yields since 1920 (Refs. 41, 42, and 43). Similarly, genetic improvements of plants in sexually compatible populations through conventional breeding have been estimated to account for half the increase in wheat yields from 1954 to 1979, almost two-fifths of the increase in sorghum yields from 1950 to 1980 (Refs. 44, 45, and 46). This exemption of plant-incorporated protectants derived through conventional breeding from sexually compatible plants will allow the type of genetic modifications leading to these types of yield gains to continue with very minimal regulatory requirements.

b. *Growers.* Growers who use plant-incorporated protectants derived through conventional breeding from sexually compatible plants should be

able to maintain or increase their productivity. Use of these plant-incorporated protectants could translate into lower grower costs because growers will use fewer inputs. Growers should be able to reduce the amount and type of chemical pesticides applied to a crop. Chemical costs, energy costs (e.g., use of tractor) and labor expenditures will be lower if the number of chemical pesticide applications decrease (Refs. 47, 48, and 49). This category of plant-incorporated protectants may also offer economic benefits to growers in circumstances where traditional pesticides may not be as effective. For example, because plant-incorporated protectants are produced and used in plants, they may be more useful for combating pests that act systemically (e.g., stalk borers) than are some traditional pesticides sprayed on the plant.

c. *Consumers.* Lower food prices for consumers are anticipated through use of plant-incorporated protectants derived through conventional breeding from sexually compatible plants, because the use of these plant-incorporated protectants may contribute to, or help maintain, yield increases. If yields increase, the supply of food should also increase. Consumer purchasing power could potentially increase with the decrease in food prices.

d. *Environment.* Environmental benefits associated with the use of plant-incorporated protectants derived through conventional breeding from sexually compatible plants include reduction in the use of chemical pesticides. These chemical pesticides may not be environmentally benign (Refs. 47, 48, and 49). Assuming that growers reduce the number and type of chemical pesticide applications, field workers would have reduced exposure. Other problems associated with chemical pesticide use such as spray drift to other crops or plants, exposure of nontarget species, groundwater contamination and spills could also be reduced.

In addition, breeding programs that develop varieties with, for example, increased yield, better resistance to pests, and better nutritional quality, could be part of an approach to agriculture that would decrease some of the impacts of agriculture on the environment while continuing to supply food to the growing human population. For example, breeding programs that increase crop yields could reduce some of the future impacts of agriculture by decreasing the amount of additional land that would have to be brought into agricultural production to feed the growing human population. The exemption described in this document would allow breeding activities among plants in sexually compatible populations through conventional breeding to continue while imposing minimal burden.

Finally, by exempting those plant-incorporated protectants unlikely to result in novel exposures, EPA is concentrating its regulatory efforts on those plant-incorporated protectants about which less certainty exists with regard to the risk that would result from the use of the plant-incorporated protectant. EPA would, for example, focus its efforts on plant-incorporated protectants such as the toxin from a spider. This toxin is targeted for the insect prey of the spider mite. Plants are not known to produce this toxin in nature or in cultivation. If this toxin were to enter the gene pool of a plant, organisms that associate with the plant and that had never previously been exposed to the toxin could now be exposed. Prior to the introduction of the toxin into these plants, only the insect prey of the spider would potentially be exposed to the toxin. If plants could now express the toxin, a different or larger group of organisms could be exposed to it, possibly resulting in adverse effects to these organisms. For example, if the toxin is found in pollen, pollinators could be exposed to the toxin. By concentrating its regulatory efforts in this way, EPA more efficiently uses its own resources.

viii. *Reporting of adverse effects for exempted plant-incorporated protectants.* EPA has decided to adopt its proposed reporting requirement for otherwise exempt plant-incorporated protectants. Under 40 CFR 174.71, anyone who produced an otherwise exempt plant-incorporated protectant will be required to report any adverse effects associated with the testing or use of the exempted plant-incorporated protectant. Failure to comply with 40 CFR 174.71 would be an unlawful act under FIFRA section 12(a) and could result in monetary penalties pursuant to FIFRA section 14.

As discussed throughout this preamble, EPA's analysis of the potential risks has led it to conclude that the plant-incorporated protectants that are the subject of this exemption present a low probability of risk. But the Agency cannot rule out completely the possibility of adverse effects to human health or the environment from the testing and use of this large category of exempted plant-incorporated protectants. The Agency cannot foresee all potential adverse effects to human health and the environment that may potentially arise for testing and use of specific plant-incorporated protectants. This is compounded by the fact that the exemption is broad, covering literally thousands of potential substances, some of which have the potential to be toxic (Ref. 8, for example). The reporting requirement is meant to address such unforeseeable events resulting from the use of these pesticides.

After weighing the remaining low probability of potential risks against the potential benefits of the plant-incorporated protectants within this category, EPA determined that the risks outweighed the benefits in the complete absence of regulatory oversight. Even though the potential benefits are very high, and the likelihood of risks are estimated to be low, the nature of the potential hazard, a toxicant(s) in the food supply, is extremely significant. Moreover, these products present issues not seen with traditional pesticides: the potential for spread of the plant's genetic material. Because plants can reproduce sexually and/or asexually, the ability to produce the plant-incorporated protectant could spread through the agro- or natural ecosystems, particularly if wild relatives acquire the ability to produce the plant-incorporated protectant through successful hybridization. In addition, the extremely large category of substances that will be exempt itself adds some degree of uncertainty to the Agency's finding. EPA continues to believe that such risks are likely to be extremely rare. However, these considerations would outweigh even the benefits of the plant-incorporated protectants that are the subject of this exemption in the absence of regulatory oversight.

However, as discussed in Unit VII.D.5., EPA does not believe that these risks justify requiring these products to be subject to the full degree of regulatory oversight under FIFRA. Rather, taking into account the very low probability of the risks, EPA believes that the post-market requirement to report adverse effects, when taken with the condition of the FFDCA exemption limiting the level of toxicants, represents a sufficient degree of oversight to allow the Agency to determine that the benefits outweigh the risks. The reporting requirement at 40 CFR 174.71 is a means of ensuring that EPA and FDA can address any potential hazard, and that the Agency's data base with respect to such products is as complete as possible. The costs of reporting are low for the regulated community, being calculated at $669.00 per notification, with EPA anticipating three adverse effects reports in 20 years,

but, as noted in the preceding paragraph, among other benefits, it will provide a mechanism that will allow EPA and FDA to react quickly to address the hazard, in the unlikely event it should arise. (See the Economic Assessment for this rule (Ref. 50)). Therefore, to ensure that there will be no unreasonable adverse effects on the environment from the plant-incorporated protectants that are the subject of this exemption, EPA is including in this final rule the reporting requirement codified at 40 CFR 174.71.

a. *Comments on the reporting requirement.* The majority of comments supported the Agency's proposal. Two of these comments noted that traditionally bred plants are monitored, both formally and informally, for desirable properties, as well as for pests and disease, and suggested that the Agency include a ''sunset clause'' in the requirement.

One comment disagreed with the adverse effects reporting requirement and pointed out that the language of the proposed rule has the potential of bringing in numerous reports of effects that are not due to the plant-incorporated protectant.

EPA carefully examined the comments it received on the proposed adverse effects reporting requirement, including comments received from other Federal agencies during the review process for this rule. In establishing this reporting requirement EPA took into account the need to target the requirement so that to the extent possible the Agency would not receive numerous reports of effects that are not due to the plant-incorporated protectant. On the other hand, guidance on what to report that is too specific would be counterproductive given that the purpose of the requirement is to be able to monitor for unforeseen events. EPA balanced all of these considerations in developing its final adverse effects reporting requirement at 40 CFR 174.71.

EPA will not adopt a ''sunset clause'' for this requirement, i.e., a clause that would designate a period of time after which information regarding adverse effects would no longer need to be reported to EPA. EPA appreciates that plant breeders monitor for properties such as yield, nutrients and resistance to pests. However, EPA does not have adequate information on which to base such a clause. The commenters do not define the parameters of the suggested ''sunset clause.'' In addition, records would probably have to be kept to know when reports would no longer be required for a particular plant-incorporated protectant, adding an additional level of complexity to the requirement. Finally, EPA believes that adverse effects reporting for otherwise exempt plant-incorporated protectants should be the responsibility of persons who produce plant-incorporated protectants for sale or distribution. Plant breeders are not necessarily involved in sale and distribution activities, and thus their access to information that an adverse effect may have occurred may be limited.

With regard to the concern expressed with respect to over-reporting, EPA recognizes that the proposed regulatory text (59 FR 60535) could have led to the submission of information that was not relevant to EPA's primary concern of adverse effects caused by the plant-incorporated protectant. In addition, the proposed requirement would have applied to some persons who would not necessarily be in a position to know if adverse effects had occurred. Therefore, EPA has revised the language of the regulatory text at 40 CFR 174.71 of the final rule to clarify that the Agency's intention is to provide a mechanism for reporting information on adverse effects related to a plant-incorporated protectant in a plant, and that only persons who ''produce'' plant-incorporated protectants for sale and distribution are responsible for submitting information to EPA. This requirement applies to the person who manufactures, for sale or distribution, a plant-incorporated protectant. It does not apply, for example, to researchers performing field experiments, nor to breeders making crosses among plant varieties with the goal of developing new plant varieties, nor to a person who only sells propagative materials (e.g., seed) to farmers without producing the propagative materials themselves.

During interagency discussion on this final rule, the question was posed of whether the commonly observed phenomenon of emergence of resistance in a pest population to one variety of plant, which necessitates the replacement of that one variety by another variety of the same crop plant, would be considered reportable by EPA under 40 CFR 174.71. EPA recognizes that this phenomenon occurs continually in agriculture and is one of the primary reasons that conventional plant breeding programs were instituted and continue to be needed by farmers. Plant breeders must continually develop plant varieties to counter the evolution in pest populations of the ability to be able to successfully attack a previously resistant variety. EPA, when it evaluated plants in sexually compatible populations for potential exemption from the requirements of FIFRA, took this phenomenon into account. Although in some instances, e.g., for Bt plant-incorporated protectants, the evolution of resistance to a pesticide in pest populations is of concern (Ref. 51), based on the history of plant breeding, adaptation between pest and plants in populations of sexually compatible plants derived through conventional breeding should not trigger adverse effects reporting under § 174.71.

b. *Guidance on adverse effects reporting.* To further address the comment that this requirement may lead to over-reporting, EPA has clarified both the procedures for reporting and the types of incidents that must be reported to meet the reporting requirement at 40 CFR 174.71. The text at 40 CFR 174.71 describes the conditions under which reporting should occur, the information which, if available, should be provided in the report, and where the reports should be directed at the EPA. In addition, EPA intends to develop specific guidance to provide further assistance to avoid confusion and unnecessary reporting. For example, the guidance would reiterate that this final rule does not require researchers to notify or consult with EPA, unless they are selling or distributing the plant-incorporated protectant to the public. As indicated previously, producers who sell or distribute an otherwise exempt plant-incorporated protectant must only notify EPA if they have information on actual adverse effects. Furthermore, this final rule does not require anyone, including researchers, to maintain any records.

EPA, in developing the adverse effects reporting requirement at 40 CFR 174.71 for otherwise exempt plant-incorporated protectants, was cognizant that in rare circumstances unanticipated effects may occur with a plant-incorporated protectant. For example, although the Agency judges it highly unlikely, it is possible that a celery variety expressing, for pesticidal purposes, high enough levels of psoralen, to cause dermatitis in humans, could arrive on the market. A celery variety expressing such levels emerged from the varietal development programs once in the past 50 years (Ref. 7). It is to enable the Federal government to address quickly circumstances of this magnitude that EPA implements the reporting requirement at § 174.71 for otherwise exempt plant-incorporated protectants.

If the producer believes the effect is due to consumption of a food but is unsure whether the effect was due to a plant-incorporated protectant, the incident must still be reported to EPA. While reports on human health would be made to EPA, EPA will share such reports with FDA, and EPA and FDA

will make a determination of whether any action is necessary to protect the public health, and if so, what constitutes appropriate action.

c. *Relationship of 40 CFR 174.71 reporting requirement to other reporting requirements.* The reporting requirements imposed upon registrants under FIFRA section 6(a)(2) for registered pesticides (including registered plant-incorporated protectants), and under 40 CFR 152.50(f)(3) for applicants for a registration are not affected by this provision. Nor would either 6(a)(2) or 40 CFR 152.50(f)(3) apply to those who would be subject to 40 CFR 174.71.

5. *Statutory finding.* EPA concludes that plant-incorporated protectants, derived through conventional breeding from plants sexually compatible with the recipient plant, as described at 40 CFR 174.25, warrant exemption under FIFRA section 25(b) because these substances are of a character that is unnecessary to be subject to FIFRA in order to carry out the purposes of the Act. EPA makes this finding with respect to both active and inert ingredients derived through conventional breeding from sexually compatible plants.

As discussed above, EPA has determined that plant incorporated protectants derived through conventional breeding from sexually compatible plants, pose a low probability of risk to humans and the environment. As explained in this preamble, and in the tolerance exemptions for the residues of such plant-incorporated protectants published elsewhere in this issue of the **Federal Register**, EPA has determined that there is a reasonable certainty that no harm will result from aggregate exposure to the residues of such products, including all anticipated dietary residues and all other exposures for which there is reliable information. EPA has also determined that these pesticide products pose a low probability of non-dietary risks to humans and the environment. The Agency bases these conclusions on information from the fields of plant genetics, plant physiology, phytopathology, microbial ecology, ecology, biochemistry, and plant breeding, supplemented by the hundreds, if not thousands, of years of experience growing and consuming plants that contain the substances that are the subject of this exemption, and by Agency knowledge of horticultural and agricultural practices.

EPA has also determined that the use of plant-incorporated protectants is not likely to cause unreasonable adverse effects on the environment in the absence of regulatory oversight other than the adverse effects reporting requirement at 40 CFR 174.71.

The remaining low probability of risks, both dietary and non-dietary human risk, as well as all environmental risks, were weighed against the potential benefits to determine whether, these remaining risks outweigh the benefits in the absence of regulatory oversight. Despite the very low level of remaining risks, and the significant potential benefits, EPA concluded that the balance between the two was extremely close. This was based on several considerations. First, the action at issue is an exemption, which could complicate EPA's ability to respond in the unlikely event a problem should arise. Moreover, the nature of the potential risks of these products themselves present particular regulatory challenges. Both the nature of the possible hazards and the exposure considerations presented by the potential for the plant's genetic material to spread to wild relatives, weigh heavily in any risk benefit balance. In addition, because it is an exemption, EPA bears the burden of both adducing the necessary evidence to support the rulemaking, and ensuring that the facts continue to support the exemption over time. Given the breadth of the exemption, EPA believed that it could not ensure over time that it could continue to support a finding that the benefits outweigh the risks in the complete absence of regulatory oversight.

But EPA does not believe that the potential risks outweigh the benefits to a degree that would warrant the pre-market approval system of registration. As described throughout this preamble, even though the nature of the risks are substantial, the probability of the risks is slight. In general, EPA believes that, given the probability of the potential risks there would be a minimal societal benefit in imposing the full degree of pre-market and post-market oversight associated with FIFRA registration. Rather, EPA believes that the imposition of the adverse effects reporting requirement, when taken with the other conditions of the FIFRA and FFDCA exemptions, tips the balance of the risks and benefits. The reporting requirement will allow the Agency to ensure that the exempted plant-incorporated protectants will continue to meet the conditions of the exemption, and will provide a mechanism to monitor the effects of this class of products. Further, because the exemption is expressly conditioned on the levels of the pesticidal substance remaining at levels that will not be injurious or deleterious to human health, EPA and FDA will be able to address the risk presented by a particular plant-incorporated protectant should a toxicant or high levels of a toxicant occur in the food supply, without the need to revoke the exemption. This permits some continuing degree of post-market oversight analogous to that provided through the registration process.

E. Establishment of 40 CFR Part 174

EPA received three comments addressing the establishment of new 40 CFR part 174. All of the comments supported the Agency's proposed rule.

As proposed in the 1994 **Federal Register** document, EPA establishes a new 40 CFR part 174. The new part will consolidate regulations specifically applicable to plant-incorporated protectants into one part of the CFR. EPA believes that establishment of a new part specifically for plant-incorporated protectants is appropriate and justified because of the characteristics that distinguish plant-incorporated protectants from other types of pesticides. This consolidation is expected to benefit the public by providing greater focus, enhanced clarity and ease of use. The regulatory requirements found in 40 CFR part 174 apply to plant-incorporated protectants only. Regulations in 40 CFR part 174 supersede other pesticide regulations found in 40 CFR parts 150 through 173 and 40 CFR parts 177 through 180 when these regulations conflict with a regulation in 40 CFR part 174. Unless otherwise superseded by 40 CFR part 174, the regulations in 40 CFR parts 150 through 173 apply to plant-incorporated protectants.

In this final rule, EPA establishes subparts in 40 CFR part 174 to contain either regulations EPA is implementing through this rule, or regulations EPA may implement in the future, tailored to apply specifically to plant-incorporated protectants. EPA has numbered and organized 40 CFR part 174 somewhat differently in this final rule than proposed in the November 23, 1994, **Federal Register** document (59 FR 60533), in part to provide greater flexibility for including future regulations at 40 CFR part 174, and for greater ease of use.

In 40 CFR part 174, subpart A, ''General Provisions,'' § 174.1 describes the scope and purpose of part 174. For clarification, some revisions have been made to the language of proposed § 174.1 as it appeared in proposed subpart A of the November 23, 1994, **Federal Register** document (59 FR 60534). Subpart A also contains at

§ 174.3 the definitions relevant to plant-incorporated protectants. As described elsewhere in this document, some definitions proposed at § 174.3 in the November 23, 1994, **Federal Register** document (59 FR 60534) were revised for clarity, to limit the exemption, and to accommodate the change of name of this type of pesticide from ''plant-pesticide'' to ''plant-incorporated protectant.'' Subpart A also describes at § 174.9 procedures for dealing with confidential business information (CBI) claims for plant-incorporated protectants.

Subpart B is established in 40 CFR part 174 and describes at § 174.21 ''General qualifications for exemptions.'' The exemption promulgated with this final rule is described at § 174.25, ''Plant-incorporated protectant derived from sexually compatible plant.'' The proposed rule in the November 23, 1994, **Federal Register** document (59 FR 60535) described the proposed exemption in proposed subpart A at § 174.5. The exemption has been described in a separate subpart B, in the final rule, to facilitate ease of use and ability to easily expand the list of exemptions.

Subpart D is established in 40 CFR part 174 for monitoring and recordkeeping requirements and sets forth requirements for submission of information regarding adverse effects caused by otherwise exempted plant-incorporated protectants. In the November 23, 1994, **Federal Register** document (59 FR 60535) the proposed language describing this proposed reporting requirement appeared at proposed 40 CFR 174.7. A subpart D has been established and the adverse effects reporting requirement has been placed at § 174.71 in subpart D to establish a distinct subpart for monitoring and recordkeeping requirements. The establishment of this subpart should facilitate ease of use by the regulated community.

Subpart C is established and reserved in 40 CFR part 174 for registration procedures and requirements. Similarly, subparts E through V are established and reserved in 40 CFR part 174 for regulations addressing other activities associated with plant-incorporated protectants; e.g., labeling, data requirements and experimental use permits. It is anticipated that future rulemakings will address these activities specifically for plant-incorporated protectants, and that the final regulations for these activities will be placed in these subparts.

Subpart W is established in 40 CFR part 174 to contain tolerances and exemptions from the requirement of a tolerance for plant-incorporated protectants under FFDCA section 408. Because 40 CFR part 174 did not exist at the time of the publication of the proposals to exempt certain categories of residues of plant-incorporated protectants (59 FR 60535, 60542, 60545) from the FFDCA requirement of a tolerance, the proposals were presented as amendments to 40 CFR part 180. With the establishment of 40 CFR part 174 through this final rule, the exemptions from the requirement of a tolerance published in companion documents elsewhere in this issue of the **Federal Register** are listed at 40 CFR 174.475, ''Nucleic acids that are part of a plant-incorporated protectant; exemption from the requirement of a tolerance'', and at § 174.479, ''Pesticidal substance derived from sexually compatible plant; exemption from the requirement of a tolerance''. Tolerances or exemptions from the requirement of a tolerance issued for plant-incorporated protectants prior to establishment of 40 CFR part 174 and thus currently listed at 40 CFR part 180 will be moved in the near future to 40 CFR part 174, subpart W. It is anticipated that establishment of subpart W in 40 CFR part 174 will facilitate ease of the use of the CFR for the general community, particularly those manufacturing and using plant-incorporated protectants.

A subpart X is established in 40 CFR part 174 and titled ''List of Approved Inert Ingredients.'' At § 174.485 EPA, EPA lists inert ingredients from sexually compatible plants.

F. Upfront Substantiation of Confidential Business Information

EPA continues to believe that substantiation of CBI claims for plant-incorporated protectants at the time of submission of information to the Agency will help to ensure a timely response to submissions for plant-incorporated protectants, further the public's right to access information and, consistent with FIFRA, protect confidential business information. EPA has concluded that up-front substantiation of CBI claims does not invalidate or jeopardize legitimate CBI claims. The Agency recognizes that the regulated community has a legitimate and legally cognizable interest in protecting trade secrets and other CBI. EPA has concluded that the requirement at 40 CFR 174.9 in the final rule allows the Agency to respond to requests for access to information, provide (where appropriate) expurgated copies of submissions and a rationale for any exclusions, and where necessary, make final determinations with respect to the validity of CBI claims without delaying regulatory action while CBI claims are being substantiated.

The release of information prior to registration is controlled in part by the Freedom of Information Act (FOIA), 5 U.S.C. 552, and section 10 of FIFRA (7 U.S.C. 136h). FOIA requires Federal agencies to provide the public with copies of agency records upon request, but contains exemptions from disclosure. Among those exemptions is one for ''trade secrets and commercial or financial information obtained from a person and privileged or confidential'' (5 U.S.C. 552(b)(4)). FIFRA section 10(b) requires protection of the same class of information. However, section 10(d)(1) limits confidentiality protection for safety and efficacy data (unless disclosure of such data in turn would disclose manufacturing or quality control processes, the method for detecting any deliberately added inert ingredient, or the identity or percentage quality of any deliberately added inert ingredient) for registered or previously registered pesticides (7 U.S.C. 136h(d)(1)). Even these excepted categories must meet the section 10(b) requirements in order to be protected. Section 3(c)(2)(A) of FIFRA provides for disclosure of certain non-confidential data 30 days after registration (7 U.S.C. 136a(c)(2)(A)).

The Agency received five comments that address the proposed requirement for up-front substantiation of CBI. Four commenters agreed with the provision. These commenters generally agreed that up-front substantiation of CBI claims will help to both ensure that the public has adequate access to information and provide timely responses to the regulated community.

One commenter disagreed with the provision for up-front substantiation of CBI. The commenter suggested that data developers would suffer substantial harm to their competitive position if data were released prematurely and asserted that EPA does not have the authority to release data to the public prior to a registration decision.

After considering these comments, EPA continues to believe that up-front substantiation of CBI claims is warranted and includes such a provision at 40 CFR 174.9. The commenter incorrectly implies that § 174.9 authorizes release of information entitled to confidential protection. All § 174.9 does is accelerate the process for determining whether information claimed as confidential is, in fact, entitled to protection under FIFRA section 10(b). Congress did not provide for absolute protection of pesticide information prior to registration; rather, it required the Agency to protect that

information which lies within the ambit of section 10(b) (7 U.S.C. 136h).

The proposed rule contained a provision that substantiations that themselves were claimed as confidential would be presumptively treated as CBI by the Agency and would not be disclosed except where ordered by a Federal court, in accordance with 40 CFR 2.205(c) (part of EPA's general confidentiality regulations at 40 CFR part 2, subpart B). This proposed provision would not have changed EPA's practice in any way; it merely echoed the pre-existing agency-wide treatment of CBI substantiations. Recently, however, the Agency proposed to amend 40 CFR 2.205(c), to eliminate the automatic protection of CBI substantiations that are themselves claimed confidential (65 FR 52684, August 30, 2000). EPA believes that such treatment of substantiations is no longer necessary to support the original purpose of the regulation, i.e., encouraging businesses to provide sufficient information to support their claims. Because the Agency is contemplating removing § 2.205(c) and because the proposed provision in 40 CFR 174.9 merely echoes the existing more general provision in § 2.205(c), the § 174.9 provision is not included in this final rule.

VIII. Documents in the Official Record

As indicated in Unit I.B.2., the official record for this rule has been established under the docket control number OPP–300369B, the public version of which is available for inspection as specified in Unit I.B.2.

A. References

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B. Additional Information

The official record for this rulemaking includes:

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 Through Conventional Breeding 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–300370B for the document entitled ''Plant-Incorporated Protectants; Supplemental Notice of Availability'' (FRL–6760–4).

The docket identified by the docket control number OPP–300369B for this document [FRL–6057–7].

Also include in the official record are:

1. Public comments submitted in response to the proposals and supplemental documents cited in the above paragraph.

2. Reports of all meetings of the Biotechnology Science Advisory Committee and the FIFRA Science Advisory Panel pertaining to the development of this final rule.

3. The Economic Analysis for this final rule, and supporting documents (Ref. 50).

4. Support documents and reports.

5. Records of all communications between EPA personnel and persons outside EPA pertaining to the final rule. (This does not include any inter-agency 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 the development of this final rule (Ref. 2).

IX. Statutory Review Requirements

In accordance with FIFRA section 25(a), this proposed rule was submitted to the FIFRA Scientific Advisory Panel, the Secretary of Agriculture (USDA), and appropriate Congressional Committees. The Scientific Advisory Panel waived its review of this final rule. Any changes made in response to comments received from USDA have been documented in the public version of the official record, along with any other comments received during the inter-agency review under Executive Order 12866.

X. Regulatory Assessment

A. Executive Order 12866

Pursuant to Executive Order 12866 (58 FR 51735, October 4, 1993), it has been determined that this is a ''significant regulatory action'' because it may raise potentially novel legal or policy issues arising out of legal mandates, the President's priorities, or the principles set forth in the Executive Order. Therefore, this action was submitted to OMB for review, and any comments or changes made during that review have been documented in the public version of the official record for this rulemaking.

EPA has prepared an economic analysis of the impacts related to this final action, which evaluates the direct costs of regulating certain types of plant-incorporated protectants and exempting one specific type of plant-incorporated protectants from FIFRA requirements (40 CFR part 174) and discusses the non-quantifiable benefits of this action. Direct compliance costs include cost estimates for the requirements to substantiate CBI when the claim is made and adverse effects reporting for otherwise exempt plant-incorporated protectants. This economic analysis is contained in a document entitled ''Economic Analysis: Regulations for Plant-Incorporated Protectants Under the Federal Insecticide, Fungicide, and Rodenticide Act,'' hereinafter ''the EA.'' This document is available as a part of the public version of the official record for this rulemaking (Ref. 50) and is briefly summarized here. (See Unit I. for instructions on obtaining support documents).

The EA presents the potential costs and benefits associated with the various requirements considered by the Agency during the development of the final action. This rule may impose direct compliance costs of $2.4 million in year 1 and $7.9 million in year 10. The benefits include the non-quantifiable benefits of assurance of protection of the environment, a more certain regulatory climate for industry, and reassurance to the public of the safety of these products. As such, the Agency believes that the potential annual costs associated with the exemption is minimal.

The Agency's EA at the time of proposed rule in 1994 estimated and compared the costs and benefits associated with four options, ranging from implementation of regulating few types of plant-incorporated protectants with exemptions of several types of plant-incorporated protectants, through implementation of increasing numbers of types of plant-incorporated protectants regulated and decreasing the exemptions. The EA for the final rule calculates the direct compliance costs associated with four similar options. The methodology employed in both the proposed EA and the final EA is the same. The costs of each of the four options in the final EA are lower than the costs of the four options in the EA for the proposed rule. This can, in general, be attributed to an agreement between EPA and USDA that costs for data generation would not be ''double counted'', i.e., if USDA required certain data, EPA would not count the costs of that data in its EA. Based on the Agency's experience over the past several years, EPA also lowered its estimate of the probability when more expensive, higher tiered testing would for required. The Agency also increased its estimates of projected number of plant-incorporated protectants submitted annually for registration.

This rule will also generate a wide range of non-monetized benefits for the public, the firms involved with agricultural biotechnology, the environment, nontarget organisms, and states. These benefits include greater certainty in the regulated community of the status of their plant- incorporated protectant. Because EPA issued a proposal to exempt several broad categories of plant-incorporated protectants in 1994, some uncertainty may exist in industry regarding the status of many plant-incorporated protectants under FIFRA and this uncertainty may also be a cost on industry. The final rule will clarify the status of one category of plant-incorporated protectants and thereby eliminate some of this uncertainty. With this action, firms developing and testing plant-incorporated protectants can plan ahead for timely product development and commercialization, which should, in turn, attract investors to the agricultural biotechnology sector. States will benefit by having a set of standardized Federal regulations that will be more easily conveyed, interpreted, and enforced. In addition, through this rule, EPA can help reassure the public of the safety of these types of products; registrants of plant-incorporated protectants can expend the considerable resources on research and development of products which may not be accepted by the public if EPA cannot assure their safety. Industry thus benefits by a reduction of uncertainty about the acceptability of their products and by greater market acceptance of the products.

B. Regulatory Flexibility Act (RFA)

Pursuant to section 605(b) of the Regulatory Flexibility Act (5 U. S. C. 601 *et seq.*), the Agency hereby certifies that this final rule will not have a significant economic impact on a substantial number of small entities. The factual basis for the Agency's determination is presented in the small entity impact analysis prepared as part of the economic analysis for this rule (Ref. 50), and is briefly summarized here.

For the purpose of analyzing the potential impacts of this rule on small entities, EPA used the definition for

small entities that is found in section 601 of the RFA. Under section 601, ''small entity'' is defined as: (1) A small business that meets Small Business Administration (SBA) size standards codified at 13 CFR 121.201; (2) a small governmental jurisdiction that is a government of a city, county, town, school district or special district with a population of less than 50,000; and (3) a small organization that is any not-for-profit enterprise which is independently owned and operated and is not dominant in its field. This rule is not expected to adversely impact small local governments. EPA's analysis, therefore, assesses the potential impacts on small not-for-profit organizations (i.e., universities with $5 million or less in annual revenues under the SBA size standard for SIC 8221), and small businesses i.e., small pesticides and agricultural chemical producers with 500 or less employees under SBA size standard for SIC 2879.

In determining whether a rule has a significant economic impact on a substantial number of small entities, the impact of concern is any significant adverse economic impact on small entities, since the primary purpose of the regulatory flexibility analyses is to identify and address regulatory alternatives ''which minimize any significant economic impact on [...] small entities.'' 5 U.S.C. sections 603 and 604. Thus, an agency may certify that a rule will not have a significant economic impact on a substantial number of small entities if the rule relieves regulatory burden, or otherwise has a positive economic effects on all of the small entities subject to the rule.

The aggregate potential impacts of the rule are expected to be minimal on small pesticide and other chemical manufacturers. Seed companies were not evaluated separately because the data available indicate that most seed companies have been purchased by larger, parent companies, many of which are pesticide manufacturers. The anticipated impact on universities, colleges, and professional schools cannot be determined. It appears that a majority of universities and colleges that would be expected to develop and research plant-incorporated protectants would not be small. Since small R&D firms lack the expertise and resources to produce, sell and manufacture plant-incorporated protectants, the burden of registration will not fall on specialized R&D firms. The Agency anticipates that many of the R&D firms with specialized expertise in this area will either work with or be purchased by larger firms with the expertise and financial resources to produce, sell, and/or distribute viable plant-incorporated protectants.

Information relating to this determination will be provided to the Chief Counsel for Advocacy of the SBA upon request.

C. Paperwork Reduction Act

Pursuant to the Paperwork Reduction Act (PRA), 44 U.S.C. 3501 *et seq.*, an agency may not conduct or sponsor, and a person is not required to respond to, an information collection request unless it displays a currently valid OMB control number. The OMB control numbers for EPA's regulations, after appearing in the preamble of the final rule, are listed in 40 CFR part 9, and included on the related collection instrument.

The information collection requirements contained in this final rule have been submitted to OMB for review and approval under the PRA in accordance with the procedures at 5 CFR 1320.11. The burden and costs related to the information collection requirements contained in this rule are described in an Information Collection Request (ICR) identified as EPA ICR No. 1693.02, which has been included in the public version of the official record described in Unit I.B.2., and is available electronically as described in Unit I.B.1., at http://www.epa.gov/opperid1/icr.htm, or by e-mailing a request to farmer.sandy@epa.gov. You may also request a copy by mail from Sandy Farmer, Collection Strategies Division, U.S. Environmental Protection Agency (Mail Code 2822), 1200 Pennsylvania Ave. NW., Washington, DC 20460, or by calling (202) 260–2740.

As defined by the PRA and 5 CFR 1320.3(b), ''burden'' means the total time, effort, or financial resources expended by persons to generate, maintain, retain, or disclose or provide information to or for a Federal agency. This includes the time needed for rule familiarization and to review instructions; develop, acquire, install, and utilize technology and systems for the purpose of collecting, validating, and verifying information, processing and maintaining information, and disclosing and providing information; adjust the existing ways to comply with any previously applicable instructions and requirements; train personnel to be able to respond to a collection of information; search data sources; complete and review the collection of information; and transmit or otherwise disclose the information.

The information collection requirements contained in this rule include up-front substantiation for claims of CBI for plant-incorporated protectant activities (e.g., EUP submissions, registration applications, tolerance requests, and adverse effects reporting), and for adverse effects reporting for the otherwise exempt plant-incorporated protectants. The annual respondent burden associated with the CBI substantiation and averse effects reporting for exempted plant-incorporated protectants is estimated to average 352 hours per submission, with a potential individual respondent burden of 25 hours for each CBI substantiation required, and 7.8 hours for each adverse effects reporting event. The annual respondent burden associated with the CBI substantiation for those plant-incorporated protectants that are not exempted by this rule is estimated to be 595 hours.

D. Unfunded Mandates Reform Act

Pursuant to Title II of the Unfunded Mandates Reform Act of 1995 (UMRA), Public Law 104–4, EPA has determined that this action does not contain a Federal mandate that may result in expenditures of $100 million or more for State, local or tribal governments, in the aggregate, or on the private sector in any one year. The analysis of the costs associated with this action are described in Unit X.A.

The UMRA requirements in sections 202, 204, and 205 do not apply to this rule, because this action does not contain any ''Federal mandates'' or impose any ''enforceable duty'' on State/Tribal, or local governments or on the private sector. The requirements in section 203 do not apply because this rule does not contain any regulatory requirements that might significantly or uniquely affect small governments.

E. Executive Order 13132

Executive Order 13132, entitled ''Federalism'' (64 FR 43255, August 10, 1999) requires EPA to develop an accountable process to ensure ''meaningful and timely input by State and local officials in the development of regulatory policies that have federalism implications.'' ''Policies that have federalism implications'' is defined in the Executive Order to include regulations that have ''substantial direct effects on the 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.''

This final rule does not have federalism implications, because it will not have substantial direct effects on the 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. The primary result of this action is to exempt certain pesticides from most FIFRA requirements. Thus, the requirements of section 6 of the Executive Order do not apply to this rule.

F. Executive Orders 13084 and 13175

This rule does not significantly or uniquely affect the communities of Indian tribal governments, nor does it involve or impose any requirements that affect Indian Tribes. Accordingly, the requirements of section 3(b) of Executive Order 13084, entitled *Consultation and Coordination with Indian Tribal Governments* (63 FR 27655, May 19, 1998), do not apply to this rule. 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. For the same reasons stated for Executive Order 13084, the requirements of Executive Order 13175 do not apply to this rule either.

G. Executive Order 12898

Pursuant to Executive Order 12898 (59 FR 7629, February 11, 1994), entitled *Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations*, the Agency has considered environmental justice related issues with regard to the potential impacts of this action on the environmental and health conditions in low-income and minority communities. The Agency is required to consider the potential for differential impacts on sensitive sub-populations. EPA considered available information on the sensitivities of subgroups as pertains to the exemptions. EPA concluded that no subgroup would be differentially affected. (See also the exemptions from the FFDCA section 408 requirement of a tolerance for residues of nucleic acids that are part of a plant-incorporated protectant and residues of plant-incorporated protectants derived through conventional breeding from sexually compatible plants published elsewhere in companion documents in this issue of the **Federal Register**).

H. Executive Order 13045

Executive Order 13045, entitled: *Protection of Children from Environmental Health Risks and Safety Risks* (62 FR 19885, April 23, 1997), does not apply to this rule because it is not economically significant as defined in section 3(f) of Executive Order 12866, and because the Agency does not have reason to believe that the environmental health or safety risks addressed by this action present disproportionate risks to children. The Agency has determined that the plant-incorporated protectants exempted in the rule pose only a low probability of risk to human health, including the health of infants and children, and that there is a reasonable certainty no harm will result to infants and children from aggregate exposure to residues of these plant-incorporated protectants in food. Existing information suggests there are no disproportionate effects on infants or children from dietary or other exposures. EPA's assessment and the results of its assessment for infants and children are contained in Unit IX.B.10. of companion documents published elsewhere in this issue of the **Federal Register** exempting from the FFDCA section 408 requirement of a tolerance, residues of plant-incorporated protectants derived through conventional breeding from sexually compatible plants, and residues of nucleic acids that are part of a plant-incorporated protectant.

I. Voluntary Consensus Standards

This rule does not involve a regulatory action that would require the Agency to consider 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). Section 12(d) directs EPA to use voluntary consensus standards in its regulatory activities unless to do so would be inconsistent with applicable law or otherwise impractical. Voluntary consensus standards are technical standards (e.g., materials specifications, test methods, sampling procedures, business practices, etc.). that are developed or adopted by voluntary consensus standards bodies. The NTTAA requires EPA to provide Congress, through OMB, explanations when the Agency decides not to use available and applicable voluntary consensus standards when the NTTAA directs the Agency to do so.

J. Executive Order 12630

EPA has complied with Executive Order 12630, entitled *Governmental Actions and Interference with Constitutionally Protected Property Rights* (53 FR 8859, March 15, 1988), by examining the takings implications of this rule in accordance with the ''Attorney General's Supplemental Guidelines for the Evaluation of Risk and Avoidance of Unanticipated Takings'' issued under the Executive Order.

K. Executive Order 12988

In issuing this rule, EPA has taken the necessary steps to eliminate drafting errors and ambiguity, minimize potential litigation, and provide a clear legal standard for affected conduct, as required by section 3 of Executive Order 12988, entitled *Civil Justice Reform* (61 FR 4729, February 7, 1996).

L. FIFRA section 25(a)(2)(b)

FIFRA section 25(a)(2)(b), requires that the Administrator of EPA consider such factors as ''. . . the effect of the regulation on production and prices of agricultural commodities, retail food prices, and otherwise on the agricultural economy. . .'' when issuing regulations under section 25 (7 U.S.C. 136w(a)(2)(B). The total direct compliance costs for the rule were estimated to be $2.4 in year 1 and $7.9 in year 10. Based on the 1997 Agricultural Census, total U.S. crop production was valued at $98 billion. The impact of these requirements will not have a significant impact on U.S. crop production or prices. The compliance costs of the rule will affect those who plan to register, manufacture and sell plant-incorporated protectants. This rule is expected to have a minimal impact on pesticide and other chemical manufacturers who in turn will sell the plant-incorporated protectants to agricultural producers. Factors, other than this rule, that occur as a result of the production of genetically altered products (i.e., consumer acceptance and the international market desire to separately market genetically altered products in the market) may affect agricultural producers and international markets. This rule may provide some benefits to the agricultural industry by helping to ensure the public on the safety of these products and positively affect consumer acceptance.

M. Executive Order 13211

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.

XI. Submission to Congress and the Comptroller General

The Congressional Review Act, 5 U.S.C. 801 *et seq.*, as added by the Small Business Regulatory Enforcement

Fairness Act of 1996, generally provides that before a rule may take effect, the Agency promulgating the rule must submit a rule report, which includes a copy of the rule, to each House of the Congress and the Comptroller General of the United States. EPA will submit a report containing this rule and other required information to the U. S. Senate, the U. S. House of Representatives and Comptroller General of the United States prior to publication of the rule in the **Federal Register**. This rule is not a ''major rule'' as defined by 5 U.S.C. 804(2).

List of Subjects in 40 CFR Parts 152 and 174

Environmental protection, Administrative practice and procedures, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: July 12, 2001.

Christine T. Whitman,

Administrator.

Therefore, 40 CFR chapter I is amended as follows:

1. By amending part 152 as follows:

PART 152—[AMENDED]

a. The authority citation for part 152 continues to read as follows:

Authority: 7 U.S.C. 136–136y; subpart U is also issued under 31 U.S.C. 9701.

b. § 152.1 is revised to read as follows:

§ 152.1 Scope.

Except as provided in part 174, part 152 sets forth procedures, requirements, and criteria concerning the registration and reregistration of pesticide products under FIFRA sec. 3, and for associated regulatory activities affecting registration. These latter regulatory activities include data compensation and exclusive use (subpart E), and the classification of pesticide uses (subpart I). Part 152 also sets forth procedures, requirements, and criteria applicable to plant-incorporated protectants. Unless specifically superceded by part 174, the regulations in part 152 apply to plant-incorporated protectants.

c. In § 152.3, by removing the paragraph designations, alphabetizing the terms, alphabetically inserting the new definitions listed below, and revising the definitions for ''active ingredient'' and ''inert ingredient'' to read as follows:

§ 152.3 Definitions.

* * * * *

Active ingredient means any substance (or group of structurally similar substances if specified by the Agency) that will prevent, destroy, repel or mitigate any pest, or that functions as a plant regulator, desiccant, or defoliant within the meaning of FIFRA sec. 2(a), except as provided in § 174.3 of this chapter.

* * * * *

Genetic material necessary for the production means both: Genetic material that encodes a substance or leads to the production of a substance, and regulatory regions. It does not include noncoding, nonexpressed nucleotide sequences.

In a living plant means inside the living plant, on the surface of the livingplant, or as an exudate from the living plant.

Inert ingredient means any substance (or group of structurally similar substances if designated by the Agency), other than an active ingredient, which is intentionally included in a pesticide product, except as provided by § 174.3 of this chapter.

* * * * *

Living plant means a plant, plant organ, or plant part that is alive, viable, ordormant. Examples of plant parts include, but are not limited to, seeds, fruits, leaves, roots, stems,flowers, and pollen.

* * * * *

Noncoding, nonexpressed nucleotide sequences means the nucleotidesequences are not transcribed and are not involved in gene expression. Examples of noncoding,nonexpressed nucleotide sequences include, but are not limited to, linkers, adapters, homopolymers, and sequences ofrestriction enzyme recognition sites.

* * * * *

Pesticidal substance, when referring to a plant-incorporatedprotectant only, means a substance that is intended to be produced and used in a living plant, or inthe produce thereof, for a pesticidal purpose during any part of a plant's life cyle (e.g., in theembryo, seed, seedling, mature plant).

Plant-incorporated protectant means a pesticidal substance that isintended to be produced and used in a living plant, or in the produce thereof, and the geneticmaterial necessary for production of such a pesticidal substance. It also includes any inertingredient contained in the plant, or produce thereof.

Produce thereof, when referring to plant-incorporated protectantsonly, means a product of a living plant containing a plant-incorporated protectant, where thepesticidal substance is intended to serve a pesticidal purpose after the product has been separatedfrom the living plant. Examples of such products include, but are not limited to, agriculturalproduce, grains, and lumber. Products such as raw agricultural commodities bearing pesticidechemical residues are not ''produce thereof'' when the residues are not intended to serve apesticidal purpose in the produce.

Regulatory region means genetic material that controls theexpression of the genetic material that encodes a pesticidal substance or leads to the production ofa pesticidal substance. Examples of regulatory regions include, but are not limited to, promoters, enhancers, andterminators.

* * * * *

d. In § 152.20, by revising paragraph (a)(1) and adding paragraph (a)(4)to read as follows:

§ 152.20 Exemptions for pesticidesregulated by another Federal agency.

* * * * *

(a) * * *

(1) Except as provided by paragraphs (a)(3) and (a)(4) of this section, all biologicalcontrol agents are exempt from FIFRA requirements.

* * * * *

(4) All living plants intended for use as biological control agents are exempt from therequirements of FIFRA. However, plant-incorporated protectants are not exempt pursuant to thissection. Regulations, including exemptions, for plant-incorporated protectants are addressed inpart 174 of this chapter.

* * * * *

2. By adding a new part 174 to read as follows:

PART 174—PROCEDURES AND REQUIREMENTS FORPLANT-INCORPORATED PROTECTANTS

Subpart A—General Provisions

Sec.

Subpart B—Exemptions

Subpart C—Registration Procedures and Requirements [Reserved]

Subpart D—Monitoring and Recordkeeping

Authority: 7 U.S.C. 136–136y; 21 U.S.C. 346a and 371.

Subpart A—General Provisions

§ 174.1 Scope and purpose.

The characteristics of plant-incorporated protectants such as their production and use inplants, their biological properties, and their ability to spread and increase in quantity in theenvironment distinguish them from traditional chemical pesticides. Therefore, plant-incorporatedprotectants are subject to some different regulatory requirements and procedures than traditionalchemical pesticides. This part sets forth regulatory requirements, criteria, and proceduresapplicable to plant-incorporated protectants under FIFRA and FFDCA. When applied toplant-incorporated protectants, the definitions and regulations in this part supercede theregulations found in parts 150 through 180 of this chapter to the extent that the regulationsconflict. Unless otherwise superceded by this part, the regulations in parts 150 through 180 of thischapter apply to plant-incorporated protectants.

§ 174.3 Definitions.

Terms used in this part have the same meaning as in FIFRA. In addition, the following termshave the meaning set forth in this section.

*Active ingredient*means a pesticidal substance that is intended to be produced and used in a living plant, or in theproduce thereof, and the genetic material necessary for the production of such a pesticidalsubstance.

Administrator means the Administrator of the United States EnvironmentalProtection Agency or his/her delegate.

Bridging crosses between plants means the utilization of anintermediate plant in a cross to produce a viable zygote between the intermediate plant and a firstplant, in order to cross the plant resulting from that zygote with a third plant that would nototherwise be able to produce viable zygotes from the fusion of its gametes with those of the firstplant. The result of the bridging cross is the mixing of genetic material of the first and third plantthrough the formation of an intermediate zygote.

Cell fusion means the fusion *in vitro* of two ormore cells or protoplasts.

Conventional breeding of plants means the creation of progenythrough either: The union of gametes, i.e., syngamy, brought together through processes such aspollination, including bridging crosses between plants and wide crosses, or vegetative reproduction. It does not include use of any of the following technologies: Recombinant DNA;other techniques wherein the genetic material is extracted from an organism and introduced intothe genome of the recipient plant through, for example, micro-injection, macro-injection, micro-encapsulation; or cell fusion.

EPA means the United States Environmental Protection Agency.

Exudate means a substance gradually discharged or secreted acrossintact cellular membranes or cell walls and present in the intercellular spaces or on the exteriorsurfaces of the plant.

FFDCA means the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321*et seq.*).

FIFRA means the Federal Insecticide, Fungicide, and Rodenticide Act, asamended (7 U.S.C. 136 *et seq.*).

Food includes articles used for food or drink by humans or otheranimals.

Food plant means a plant which either in part or *intoto*, is used as food.

Genetic material necessary for the production means both: Genetic material that encodes a substance or leads to the production of a substance; and regulatory regions. It does not include noncoding, nonexpressed nucleotide sequences.

Genome means the sum of the heritable genetic material in the plant, including genetic material in the nucleus and organelles.

In a living plant means inside the living plant, on the surface of the livingplant, or as an exudate from the living plant.

Inert ingredient, means any substance, such as a selectable marker, other than the active ingredient, where thesubstance is used to confirm or ensure the presence of the active ingredient, and includes the geneticmaterial necessary for the production of the substance, provided that genetic material isintentionally introduced into a living plant in addition to the active ingredient.

Living plant means a plant, plant organ, or plant part that is alive, viable, ordormant. Examples of plant parts include, but are not limited to, seeds, fruits, leaves, roots, stems,flowers, and pollen.

Noncoding, nonexpressed nucleotide sequences means the nucleotidesequences are not transcribed and are not involved in gene expression. Examples of noncoding,nonexpressed nucleotide sequences include, but are not limited to, linkers, adapters, homopolymers, and sequences ofrestriction enzyme recognition sites.

Nucleic acids means ribosides or deoxyribosides of adenine, thymine,guanine, cytosine, and uracil; polymers of the deoxyribose-5'-monophosphates of thymine,cytosine, guanine, and adenine linked by successive 3'-5' phosphodiester bonds (also known asdeoxyribonucleic acid); and polymers of the ribose-5'-monophosphates of uracil, cytosine, guanine, and adenine linked by successive 3'-5' phosphodiester bonds (also known as ribonucleic acid).The term does not apply to nucleic acid analogues (e.g., dideoxycytidine), or polymers containingnucleic acid analogues.

Pesticidal substance, means a substance that is intended to be produced and used in a living plant, orin the produce thereof, for a pesticidal purpose, during any part of a plant's life cyle (e.g., in theembryo, seed, seedling, mature plant).

Plant, for plant-incorporated protectants, means an organismclassified using the 5-kingdom classification system of Whittaker in the kingdom Plantae. Thisincludes, but is not limited to, bryophytes such as mosses, pteridophytes such as ferns,gymnosperms such as conifers, and angiosperms such as most major crop plants.

Plant-incorporated protectant means a pesticidal substance that is intendedto be produced and used in a living plant, or in the produce thereof, and the genetic materialnecessary for production of such a pesticidal substance. It also includes any inert ingredientcontained in the plant, or produce thereof.

Produce thereof, when used with respect to plants containing plant-incorporated protectants only, means a product of a living plant containing a plant-incorporatedprotectant, where the pesticidal substance is intended to serve a pesticidal purpose after theproduct has been separated from the living plant. Examples of such products include, but are notlimited to, agricultural produce, grains, and lumber. Products such as raw agriculturalcommoditiesbearing pesticide chemical residues are not ''produce thereof'' when the residues are not intendedto serve a pesticidal purpose in the produce.

Recipient plant means the living plant in which theplant-incorporated protectant is intended to be produced and used.

Recombinant DNA means the genetic material has been manipulated*in vitro* through the use of restriction endonucleases and/or other enzymes that aid in modifyinggenetic material, and subsequently introduced into the genome of the plant.

Regulatory region means genetic material that controls theexpression of the genetic material that encodes a pesticidal substance or leads to the production ofa pesticidal substance. Examples of regulatory regions include, but are not limited to, promoters, enhancers, andterminators.

Sexually compatible, when referring to plants, means a viable zygoteis formed only through the union of two gametes through conventional breeding.

Source means the donor of the genetic material that encodes apesticidal substance or leads to the production of a pesticidal substance.

Vegetative reproduction means either:

(1) In seed plants, reproduction by apomixis, or

(2) In other plants, reproduction by fragmentation, or division of the somatic body.

Wide crosses means to facilitate the formation of viable zygotesthrough the use of surgical alteration of the plant pistil, bud pollination, mentor pollen,immunosuppressants, *in vitro* fertilization, pre-pollination and post-pollination hormone treatments,manipulation of chromosome numbers, embryo culture, or ovary and ovule cultures.

§ 174.9 Confidential businessinformation claims for plant-incorporated protectant submissions.

Although it is strongly recommended that the submitter minimize the amount of dataand other information claimed as Confidential Business Information (CBI), a submitter may asserta claim of confidentiality for all or part of the information submitted to EPA in a submission for aplant-incorporated protectant. (See part 2, subpart B of this chapter.) To assert such a claim, thesubmitter must comply with all of the following procedures:

(a) Any claim of confidentiality must accompany the information at the time theinformation is submitted to EPA. Failure to assert a claim at that time constitutes a waiver ofconfidentiality for the information submitted, and the information may be made available to thepublic, subject to section 10(g) of FIFRA, with no further notice to the submitter.

(b) Any claim of confidentiality must be accompanied, at the time the claim is made,by comments substantiating the claim and explaining why the submitter believes that theinformation should not be disclosed. The submitter must address each of the points listed in§ 2.204(e)(4) of this chapter in the substantiation. EPA will consider incomplete allplant-incorporated protectant submissions containing information claimed as CBI that are notaccompanied by substantiation, and will suspend any applicable review of such submissionsuntil the required substantiation is provided.

Subpart B—Exemptions

§ 174.21 General qualifications forexemptions.

A plant-incorporated protectant is exempt from the requirements of FIFRA, other than therequirements of § 174.71, if it meets all of the following criteria:

(a) The plant-incorporated protectant meets the criteria listed in at least one of thesections in § § 174.25 through 174.50.

(b) When the plant-incorporated protectant is intended to be produced and used in acrop used as food, the residues of the plant-incorporated protectant are either exempted from therequirement of a tolerance under FFDCA (as amended, 21 U.S.C. 321 *et seq.*) ascodified at § § 174.475 through 174.479, or no tolerance wouldotherwise be required for the plant-incorporated protectant.

(c) Any inert ingredient that is part of the plant-incorporated protectant is on the listcodified at § § 174.485 through 174.490.Plant-incorporated protectants that are not exempt from the requirements of FIFRA under thissubpart are subject to all the requirements of FIFRA.

§ 174.25 Plant-incorporated protectantfrom 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 theproduction of the pesticidal substance is from a plant that is sexually compatible with the recipientplant.

(b) The genetic material has never been derived from a source that is not sexuallycompatible with the recipient plant.

Subpart C—Registration Procedures and Requirements [Reserved]

Subpart D—Monitoring and Recordkeeping

§ 174.71 Submission of informationregarding adverse effects.

(a) Any person who produces, for sale or distribution, a plant-incorporated protectantexempt under subpart B of this part, who obtains any information regarding adverse effects onhuman health or the environment alleged to have been caused by the plant-incorporated protectantmust submit such information to EPA. This requirement does not apply to any person who does not produce a plant-incorporated protectant exempt under supart B of this part. This may include, for example, researchers performing field experiments, breeders making crosses among plant varieties with the goal of developing new plant varieties, or a person who only sells propagative materials (e.g., seed) to farmers without producing the propagative materials themselves. EPA must receive the report within 30 calendar days of thedate the producer first possesses or knows of the information.

(b) Adverse effects on human health or the environment for purposes of plant-incorporated protectant means at a minimum information about incidents affecting humans orother nontarget organisms where both:

(1) The producer is aware, or has been informed, that a person or nontarget organismallegedly suffered a toxic or adverse effect due to exposure to (e.g., ingestion of) a plant-incorporated protectant.

(2) The producer has or could reasonably obtain information concerning where theincident occurred.

(c) All of the following information, if available, must be included in a report.

(1) Name of reporter, address, and telephone number.

(2) Name, address, and telephone of contact person (if different than reporter).

(3) Description of incident.
(4) Date producer became aware of incident.
(5) Date of incident.
(6) Location of incident.
(d) Mail reports and questions to: Biopesticides and Pollution Prevention Division (7511C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460 or deliver reports and questions to: Crystal Mall #2, Room 910, 1921 Jefferson Davis Hwy., Arlington, VA.

Subparts E—F [Reserved]

Subpart G—Labeling [Reserved]

Subpart H—Data Requirements [Reserved]

Subpart I—[Reserved]

Subpart J—Good Laboratory Practices [Reserved]

Subpart K—Export Requirements [Reserved]

Subparts L—T [Reserved]

Subpart U—Experimental Use Permits [Reserved]

Subpart V—[Reserved]

Subpart W–Tolerances and Tolerance Exemptions

§ 174.451 Scope and purpose.

This subpart lists the tolerances and exemptions from the requirement of a tolerancefor residues of plant-incorporated protectants in or on raw agricultural commodities, in food, andin animal feeds.

Subpart X—List of Approved Inert Ingredients

§ 174.480 Scope and purpose.

This subpart lists the inert ingredients that have been exempted from FIFRA andFFDCA section 408 requirements and may be used in a plant-incorporated protectant listed insubpart B of this part.

§ 174.485 Inert ingredients from sexually compatible plant.

An inert ingredient, and residues of the inert ingredient, are exempt if all of the following conditions are met:
(a) The genetic material that encodes the inert ingredient or leads to the production of the inert ingredient is derived from a plant sexually compatible with the recipient food plant.
(b) The genetic material has never been derived from a source that is not sexually compatible with the recipient food plant.
(c) The residues of the inert ingredient are not present in food from the plant at levels that are injurious or deleterious to human health.

Subparts Y—Z [Reserved]

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ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 174

[OPP–300371B; FRL–6057–5]

RIN 2070–AC02

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)

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: The substances plants produce for protection against pests, and the genetic material necessary to produce these substances, are pesticides under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), if humans intend to use these substances for ''preventing, destroying, repelling or mitigating any pest.'' These substances, produced and used in living plants, along with the genetic material necessary to produce them, are also ''chemical pesticide residues'' under the Federal Food, Drug, and Cosmetic Act (FFDCA). EPA calls these substances along with the genetic material necessary to produce them, ''plant-incorporated protectants.'' In this final rule, EPA exempts from the FFDCA section 408 requirement of a tolerance, residues of nucleic acids that are part of a plant-incorporated protectant. Nucleic acids are ubiquitous in all forms of life, have always been present in human and domestic animal food and are not known to cause any adverse health effects when consumed as part of food. EPA believes there is a reasonable certainty that no harm will result from aggregate exposure to residues of nucleic acids that are part of a plant-incorporated protectant.

DATES: This regulation is effective September 17, 2001. Objections and requests for hearings must be received by EPA on or before September 17, 2001.

ADDRESSES: Written objections and hearing requests may be submitted by regular mail, electronically, or in person. Follow the detailed instructions for the regular mail and in person methods in Unit II. of the **SUPPLEMENTARY INFORMATION**.

FOR FURTHER INFORMATION CONTACT: By mail: Philip Hutton, Biopesticides and Pollution Prevention Division, Office of Pesticide Programs (7511C), Environmental Protection Agency, 1921 Jefferson Davis Highway, Arlington, VA 22202; telephone number: (703) 308–8260; e-mail address: hutton.phil@epa.gov.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Document 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