

**ENVIRONMENTAL PROTECTION  
AGENCY**
**40 CFR Part 180**
**[OPP-300368A; FRL-5717-2]**
**RIN 2070-AC02**
**Plant-Pesticides; Supplemental Notice  
of Proposed Rulemaking**
**AGENCY:** Environmental Protection Agency (EPA).

**ACTION:** Supplemental notice of proposed rulemaking.

**SUMMARY:** This document announces the availability of information for additional public comment regarding a proposed exemption from the requirement of a tolerance under the Federal Food, Drug, and Cosmetic Act (FFDCA) for pesticidal substances that are a component of certain plant-pesticides, i.e., those plant-pesticides that are derived from closely related plants. Comments on this document may also affect EPA's final determination on a proposed exemption under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) for this same category of plant-pesticides. In 1994, EPA proposed to exempt from the requirement of a tolerance the pesticidal substance portion of plant-pesticides moved between closely related plants because a tolerance would not be necessary to protect the public health. Since publication of the proposal, Congress enacted the Food Quality Protection Act (FQPA) which amended FFDCA and FIFRA. EPA is issuing this document today 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 exemption from the requirement of a tolerance for pesticidal substances moved between closely related plants. EPA believes that it considered most of the substantive issues associated with the FQPA amendments when it issued the proposals in 1994. EPA is thus, in this document, specifically seeking comment only on its evaluation of the requirements imposed by FQPA that the Agency did not address in the proposals.

**DATES:** Comments, identified by the docket control number "OPP-300368A," must be received on or before June 16, 1997.

**ADDRESSES:** By mail, submit written comments to: Public Information and Records Integrity Branch, Information Resources and Services Division (7506C), Office of Pesticide Programs, Environmental Protection Agency, 401

M St., SW., Washington, DC 20460. In person deliver comments to: Rm. 1132, Crystal Mall #2, 1921 Jefferson Davis Highway, Arlington, VA.

Comments and data may also be submitted electronically by following the instructions under Unit IV.D. of this document. No Confidential Business Information (CBI) should be submitted through e-mail.

**FOR FURTHER INFORMATION CONTACT:** By mail: Elizabeth Milewski, Office of Science, Coordination and Policy, Office of Prevention, Pesticides and Toxic Substances (7101), Environmental Protection Agency, 401 M St., SW., Washington, DC 20460, Telephone: (202) 260-6900, e-mail address: milewski.elizabeth@epamail.epa.gov.

**SUPPLEMENTARY INFORMATION:**
**I. Introduction**

EPA issued in the November 23, 1994 **Federal Register** a package of five separate **Federal Register** proposals (59 FR 60496, 60519, 60535, 60542 and 60545) (FRL-4755-2, FRL-4755-3, FRL-4758-8, FRL-4755-5, and FRL-4755-4) which together described EPA's approach to substances produced in plants that enable the plants to resist pests or disease. EPA's package of proposals indicated that these substances are pesticides under section 2 of FIFRA (7 U.S.C. 136(u)) if they are "intended for preventing, destroying, repelling, or mitigating any pest" or if they are ". . . intended for use as a plant regulator, defoliant, or desiccant" regardless of whether the pesticidal capabilities evolved in the plants or were introduced by breeding or through the techniques of modern biotechnology. These substances, and the genetic material necessary to produce them, were designated "plant-pesticides" by EPA in the November 23, 1994 **Federal Register** notices. The proposals defined a "plant-pesticide" as "a pesticidal substance that is produced in a living plant and the genetic material necessary for the production of the pesticidal substance where the pesticidal substance is intended for use in the living plant" (59 FR at 60534).

One of the five documents (59 FR 60535) proposed to exempt the pesticidal substance portion of plant-pesticides moved between closely related plants from the FFDCA (21 U.S.C. 346a) requirement of a tolerance based upon an evaluation of the potential for new dietary exposures to the substances when they are produced in plants, or in plant parts, used as food or feed. EPA proposed in the same **Federal Register** (59 FR at 60537) to define closely related plants as plants

that are sexually compatible. In the proposal, sexually compatible, when referring to plants, means capable of forming a viable zygote through the fusion of two gametes, including the use of bridging crosses and/or wide crosses. EPA stated in the proposed exemption that a tolerance is not necessary to protect the public health for these pesticidal substances because no new dietary exposures are likely to occur for pesticidal substances moved between sexually compatible plants. For pesticidal substances in this category, many years of experience of human use suggest that under normal dietary conditions these pesticidal substances present negligible risk. Specifically, EPA proposed that "residues of pesticidal substances produced in living plants as plant-pesticides are exempt from the requirement of a tolerance if the genetic material that encodes for a pesticidal substance or leads to the production of a 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" (59 FR at 60542).

This supplemental notice addresses the pesticidal substance portion of plant-pesticides produced in food plants. A companion supplemental notice issued elsewhere in today's **Federal Register** addresses the proposed exemption for the nucleic acid component of plant-pesticides with regard to the FQPA amendments to FFDCA.

Because FQPA modified FIFRA (7 U.S.C. 136 *et seq.*) by incorporating the FFDCA safety standard into the FIFRA test for determining whether a pesticide poses an unreasonable adverse effect, comments on these supplemental notices may also affect EPA's final determination on the proposed exemption (59 FR 60519) under FIFRA for plant-pesticides that are derived from plants sexually compatible with the recipient plant.

EPA is issuing this supplemental notice, as well as the companion supplemental notice on nucleic acids to ensure that the public has had adequate opportunity to comment on certain new considerations raised by the FQPA amendments to FFDCA as these considerations relate to the proposed exemption from tolerance for residues of pesticidal substances derived from sexually compatible plants. In evaluating a pesticide chemical residue for exemption from FFDCA tolerance requirements, EPA must now explicitly address certain factors, and make a determination that there is a reasonable certainty that aggregate exposure to the

residue will cause no harm to the public. The factors to be considered are iterated in Unit II. of this supplemental notice. EPA's evaluation of these factors relative to the proposed exemption (59 FR 60535) is contained in Unit IV. of this supplemental notice. Consistent with FFDCA section 408(c)(2)(B), EPA has reviewed the available scientific data and other relevant information in support of this action. In today's supplemental notice, EPA requests comment only on the new conclusions identified in Unit V.C. of this supplemental notice.

In light of FQPA, EPA is engaged in a process, including consultation with registrants, states, and other interested stakeholders, to make decisions on the new policies and procedures that will be appropriate as a result of enactment of FQPA. In establishing this exemption from the requirement of a tolerance for pesticidal substances derived from sexually compatible plants, EPA does not intend to set precedents for the application of section 408 and the new safety standard to other tolerances and exemptions. This exemption from the requirement of a tolerance will not restrict EPA's options with regard to general procedures and policies for implementation of the amended FFDCA section 408.

## II. Statutory Authority

Under FFDCA, EPA regulates pesticide chemical residues by establishing tolerances limiting the amounts of residues that may be present in food, or by establishing exemptions from the requirement of a tolerance for such residues. Pesticide chemical residues subject to regulation under FFDCA are defined by reference to the definition of pesticide under FIFRA. FFDCA section 201(q)(1) defines a "pesticide chemical residue" to mean the residue in or on food of a pesticide chemical or other added substance resulting primarily from the metabolism or degradation of a pesticide chemical (21 U.S.C. 321(q)(2)). A "pesticide chemical" means "any substance that is a pesticide within the meaning of the Federal Insecticide, Fungicide, and Rodenticide Act, including all active and inert ingredients of such pesticide" (21 U.S.C. 321(q)(1)).

FIFRA authorizes EPA to regulate the sale and distribution of pesticides in the United States and to exempt a pesticide from the requirements of FIFRA if it is not of a character requiring regulation (7 U.S.C. 136a(a) and 136w(b)). 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)).

FQPA amends both FFDCA and FIFRA. FQPA, which took effect on August 3, 1996, among other things, amends FIFRA such that a registration cannot be issued for a pesticide to be used on or in food unless the residue of the pesticide in food qualifies for a tolerance or exemption from the requirement for a tolerance. FQPA modified FIFRA section 2(bb) by incorporating the FFDCA section 408 safety standard into the test for determining whether a pesticide poses an unreasonable adverse effect (7 U.S.C. 136(bb)). 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 FFDCA. Thus, 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).

FQPA amends FFDCA section 408(c)(2)(A)(i) to allow EPA to establish an exemption from the requirement of a tolerance for a "pesticide chemical residue" only if EPA determines that the exemption is "safe" (21 U.S.C. 346a(c)(2)(A)(i)). Section 408(c)(2)(A)(ii) defines "safe" to mean 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)(ii)). This includes exposure through drinking water, but does not include occupational exposure. In establishing an exemption from the requirement of a tolerance, FFDCA section 408(c), like the statute prior to FQPA, does not require EPA to consider benefits that might be associated with use of the pesticide chemical.

FFDCA section 408 requires EPA to give special consideration to exposure of infants and children to the pesticide chemical residue in establishing an exemption and to "ensure that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue" (21 U.S.C.

346a(b)(2)(C)(ii)(I) and (c)(2)(B). Section 408(b)(2)(D) specifies other, general factors EPA is to consider in establishing an exemption. Section 408(c)(3)(B) prohibits an exemption unless there is either a practical method for detecting and measuring levels of pesticide chemical residue in or on food or there is no need for such a method (21 U.S.C. 346a(c)(3)(B)).

Specifically, EPA must consider the following in deciding whether to grant an exemption:

1. The validity, completeness, and reliability of the available data from studies of the pesticide chemical and pesticide chemical residue.
  2. Nature of any toxic effect shown to be caused by the pesticide chemical or residues in studies.
  3. Available information concerning the relationship of the results of such studies to human risk.
  4. Available information concerning the dietary consumption patterns of consumers (and major identifiable subgroups of consumers).
  5. Available information concerning the cumulative effects of such residues and other substances that have a common mechanism of toxicity.
  6. Available information concerning the aggregate exposure levels of consumers to the pesticide chemical residue and to other related substances, including dietary exposure and non-occupational exposures.
  7. Available information concerning the variability of the sensitivities of major identifiable subgroups of consumers.
  8. Such information as the Administrator may require on whether the pesticide chemical may have an effect in humans that is similar to an effect produced by a naturally-occurring estrogen or other endocrine effects.
  9. Safety factors which in the opinion of experts qualified by scientific training and experience to evaluate the safety of food additives are generally recognized as appropriate for the use of animal experimentation data (21 U.S.C. 346a(b)(2)(D)).
- Additionally, with respect to exposure of infants and children, consistent with section 408(b)(2)(C), EPA must assess the risk of the pesticide based on available information concerning:
1. Consumption patterns that are likely to result in disproportionately high consumption of food with pesticide residues.
  2. Special susceptibility of infants and children to such residues.
  3. Cumulative effects of residues with other substances that have a common

mechanism of toxicity (21 U.S.C. 346a(b)(2)(C) and (c)(2)(B)).

### III. Summary of Proposed Regulations

This supplemental notice affects three of the proposals that appeared in the November 23, 1994 **Federal Register**: (1) A proposal under FFDCA to exempt from the requirement of a tolerance, residues of the pesticidal substance portion of any plant-pesticide that is derived from a plant that is sexually compatible with the recipient plant (59 FR 60535); (2) a companion proposal (59 FR 60542) under FFDCA to exempt "residues of nucleic acids produced in living plants as part of a plant-pesticide"; and (3) a proposal (59 FR 60519) under FIFRA to exempt from most of the requirements of FIFRA, plant-pesticides derived from a plant that is sexually compatible with the recipient plant.

In the November 23, 1994 **Federal Register**, the Agency proposed to exempt from the FFDCA requirement of a tolerance (59 FR 60535) and most requirements of FIFRA (59 FR 60519) pesticidal substances moved between plants that are closely related. EPA discussed two options for describing plants that are closely related: (1) Plants that are sexually compatible, or (2) plants that are within the same taxonomic genus or are sexually compatible. Sexual compatibility would include use of techniques such as wide and bridging crosses. EPA's preferred approach for describing closely related plants was the option based on sexual compatibility alone. Thus, EPA proposed that plant-pesticides derived from plants that are sexually compatible would be exempt from most FIFRA requirements, and residues of pesticidal substances that are derived from sexually compatible plants would be exempted from the FFDCA requirement of a tolerance.

The rationale underlying the proposed exemptions is that plants in a sexually compatible population are likely to have the same information encoded in their genetic material and to share traits in common. Groups of plants having a common pool of genetic material have resulted from the processes of evolution. Generations of directed breeding to produce improved crops for cultivation have tended to increase the relatedness of agricultural crop plants and reduce the variability in the common pools of genetic information of crop plants. Because sexually compatible plants share a common pool of genetic material, movement of genetic material encoding pesticidal substances between plants in a sexually compatible population is

unlikely to result in novel environmental or dietary exposures. If a crop plant normally produces a pesticidal substance, humans consuming the crop, and organisms coming into contact with the plant, have been exposed to that substance in the past, perhaps over long periods of time. No new exposures are likely to occur. Because of the high degree of relatedness among plants comprising sexually compatible populations, the potential for new human exposures, either dietary or environmental, is low for pesticidal substances in sexually compatible plants or plant parts used as food or feed. Under the exemptions for plant-pesticides derived from sexually compatible plants, EPA exempts from the FFDCA requirement of a tolerance those plant-pesticides that are normally a component of (not new to) the recipient plant. EPA believes that crops grown for food in the U.S. today would qualify for this exemption (59 FR at 60535 and 60542) based on the standard of relatedness as described by sexual compatibility.

The proposed exemption from the requirement of a tolerance (59 FR 60535) was examined within the context of the food supply and dietary consumption. Many substances having pesticidal activity occur naturally at low concentrations in the edible parts of plants and have long been accepted as part of the human diet. Extensive use and experience show the safety of foods containing these substances. Although very large numbers of plant varieties are used and large numbers of varieties are introduced into agricultural use each year, there are only a few examples of plant varieties causing food safety concerns.

Based on these considerations, and as required by the FFDCA prior to enactment of the FQPA, EPA concluded that plant-pesticides found in the current food supply would present no hazard under potential use conditions and, hence, a tolerance would not be necessary to protect the public health.

EPA's alternative option for describing relatedness in plants (59 FR at 60537) used both sexual compatibility and taxonomy (genus). Under this alternative option, if a plant-pesticide was derived from a plant classified in the same genus as the recipient plant or if the donor plant was sexually compatible with the recipient plant, that plant-pesticide would be exempt. The assumption underlying this alternative option was that the taxonomic grouping of genus correlated to a relatively high degree of relatedness. This option was not EPA's preferred approach, because even though plants grouped within a

genus may be fairly closely related, certain species within a genus may never have contributed traits to plants currently found in the food supply and thus no known dietary exposure exists for traits from such plants. Therefore, EPA preferred the option based on sexual compatibility alone which EPA believes best describes plant-pesticides found in the food supply.

In the 1994 **Federal Register** (59 FR 60535), EPA also proposed to exempt from the requirement of a tolerance a second category of pesticidal substances. This second category consists of pesticidal substances that are derived from food plants that are not closely related to the recipient plant but which would not result in significantly different dietary exposures when produced in the recipient plant. This second category will not be addressed in this supplemental notice but will be addressed in a separate **Federal Register** in the future.

### IV. Risk Assessment and Safety Determinations

#### A. Risk Assessment in the 1994 Proposal

This section reviews the analysis that EPA used to support its 1994 proposal (59 FR 60535) to exempt pesticidal substances derived from sexually compatible plants from the requirement of a food tolerance under the FFDCA. EPA also relied upon the analysis in the 1994 FFDCA proposal to evaluate human dietary risks in support of its proposal (59 FR 60519) to exempt plant-pesticides from sexually compatible plants from most FIFRA requirements. Non-dietary human risks from exposure to such pesticidal substances were examined under the analysis for the proposed FIFRA exemption and are discussed in this supplemental notice only as they pertain to the dietary risks.

When EPA proposed in 1994 to exempt residues of pesticidal substances that are derived from sexually compatible plants from the requirement of a tolerance (59 FR 60535), it concluded that a food tolerance for such substances would not be necessary to protect the public health because such substances presented no significant hazards under potential use conditions. EPA based this conclusion upon its analysis of potential dietary exposure, hazard and risk from consumption of plants that contain these substances. EPA recognized and relied on the long history of human experience with growing and consuming plants for food and with the procedures of plant breeding. Plant breeding combines the scientific knowledge of experimental laboratory disciplines such as plant

physiology, plant genetics, and phytopathology into a practical field science that develops new plant cultivars for use in agriculture. EPA has used these bases of knowledge and experience in its estimation of exposures and hazards of the residues of pesticidal substances addressed by this supplemental notice as well as for the 1994 proposal.

EPA concluded in the 1994 proposal (59 FR 60535) that the vast majority of plant varieties developed by plant breeders using traits from sexually compatible plants produce foods that are safe for human consumption. This conclusion is based on the experience of consuming crops resulting from scientific breeding as well as the historical consumption of crops since the prehistorical origins of agriculture. These foods undoubtedly contain(ed) pesticidal substances (and the genetic material necessary to produce them) and share a history of safe consumption. In addition, appropriate processing procedures are widely known and are routinely used by consumers in preparation of food from such sources, including those foods which require specific processing/preparation steps to avoid dietary problems.

In the 1994 proposal, EPA stated that many substances having pesticidal activity occur naturally at low concentrations in the edible parts of plants and have long been accepted as part of the human diet. Extensive use and experience show the safety of foods containing these substances. For many foods, the naturally-occurring toxicants they may contain, some of which might be pesticidal in function, are known. Also, the established practices that plant breeders employ in selecting and developing new plant varieties, such as chemical analyses, taste-testing, and visual analyses, have historically proven to be reliable for ensuring food safety. That there are few documented cases of new plant cultivars causing food safety problems despite the large numbers of new varieties introduced into commerce each year, is a reflection of the effectiveness of this process (59 FR at 60538).

Plant varieties for the food market have been developed by breeders seeking better products, higher yields, and other desirable crop characteristics. In this process, it has been common agricultural practice to move traits among sexually compatible food plant varieties as well as to introduce traits from sexually compatible wild relatives into plant varieties that are used as food plants. This type of breeding process has been used on most sexually compatible crop plants, and tended to

increase the extent of relatedness among plant varieties in agricultural crops. The 1994 proposal is based on experience with the exposure of human populations to crops developed through the breeding process, i.e., crops developed through 50 to 100 years of scientific breeding among sexually compatible plant populations using Mendelian genetics. The sexually compatible, wild relatives of cultivated plants that are used in this process do not themselves necessarily have any history of human consumption but have safely contributed traits through sexual recombination to cultivars on the market. For example, wild species of tomatoes have been used, in plant breeding, as a source of increased resistance to economically important diseases in tomato (Ref. 1). Sexually compatible crop varieties of the same plant species are also crossed with each other to achieve better pest resistance in their progeny. Food plant varieties developed in this way have been introduced, cultivated, and consumed by humans for many years with very few observed adverse effects (59 FR at 60538).

If a food plant or its close relative normally produces a pesticidal substance, humans have likely been exposed to that substance in the past. Experience with both growing agricultural plants and consuming food from plants which undoubtedly contain pesticidal substances demonstrates the safety of the current food supply, including substances in the food supply that may be plant-pesticides. The Agency believes this experience combined with the knowledge of plant genetics, plant physiology, phytopathology and plant breeding are the appropriate considerations in evaluating the potential risks of residues of the pesticidal substances proposed for the tolerance exemption (59 FR 60535).

The residues of the pesticidal substances that are the subject of the proposed exemption have evolved in populations of sexually compatible plants. They are part of the metabolic cycles of these plants. They are thus subject to the processes of degradation and decay that all organic matter undergoes. They are not likely to persist in the environment nor bioaccumulate in the tissues of living organisms. Because they do not persist, the potential for new exposures to the residues to occur, beyond direct physical exposures to the plant, would be limited. As noted in the proposal (59 FR at 60516), plant-pesticides present negligible exposure of the pesticidal substances to humans outside the

dietary route because the substances are in the plant tissue and thus are found either within the plant or in close proximity to the plant. In contrast, applied synthetic chemicals have much greater potential for new dietary exposures. Prior to the use of synthetic pesticides, there may be very little scientific experience with the new pesticidal substance or even a complete lack of known dietary exposure to the pesticidal substance.

EPA evaluated the potential risks of a pesticidal substance derived from a closely-related plant relative based upon the unique characteristics of plant-pesticides. In evaluating the pesticidal substance component of plant-pesticides, EPA took into account available knowledge from a number of scientific disciplines. Experimental data in the area of plant genetics provided an estimate of the exchange, between plants, of genetic material that is necessary for the production of the pesticidal substances. EPA also considered information from the field of plant physiology regarding plant metabolism, the production of substances that may have pesticidal effects, and conditions that may limit the production of such substances. This information provided a basis for EPA's estimation of the physiological limitations to production of substances that may have a pesticidal effect. The Agency also used experimental data derived from the science of phytopathology to characterize the disease and pest resistant mechanisms known to occur in plants. All of these bases of knowledge and experience were integral to EPA's assessment of exposures and hazards associated with pesticidal substances.

EPA considered whether there are variations in the levels of pesticidal substances that are the subject of the proposed exemption (59 FR 60535) within and between plant varieties, and thus variation in exposure that might affect the Agency's determination that pesticidal substances that are the subject of the proposed exemption present negligible risk. The amount of pesticidal substance produced by plants normally varies among members of a closely related population (even within a single variety), because of the effects of conditions such as genetic constitution and environment (e.g., weather) on trait expression. This variation in turn leads to differences in the levels and types of exposure to the pesticidal substance. Since such variation is a natural phenomenon common to all plants, humans have been and are always exposed to varying levels of the pesticidal substances that are the subject

of this exemption when they consume food from plants.

EPA also considered the constraints upon the extent to which any substance can be increased in highly managed food crop plants without unwanted effects on other, desirable characteristics of the plant such as yield or palatability. In general, breeders balance a number of characteristics (e.g., yield, palatability, uniformity of seed drop) in developing marketable plant varieties. Plants have, as do all organisms, only a limited capacity to express a particular trait without an unacceptable drain on energy reserves. Greatly increased levels of a pesticidal substance would, in general, only be accomplished at the expense of expressing other agriculturally desirable traits (e.g., yield). EPA does not believe that levels of pesticidal substances that are the subject of the proposed exemption (59 FR 60535) will be increased to a point that will result in an adverse dietary effect. EPA has extensively evaluated whether quantitative changes in levels of the pesticidal substances that are the subject of the proposed exemption would warrant regulation by the setting of a food tolerance. EPA has determined that changes in the levels of these pesticidal substances present a reasonable certainty of causing no harm because the highest levels likely to be attained in plants are not likely to result in overall significantly different dietary exposures. EPA does not anticipate that attempts to increase the levels of these pesticidal substances would lead to a significantly different spectrum of exposure than that with which there is substantial experience.

The evaluation of potential dietary risk associated with the pesticidal substances that are the subject of the proposed exemption (59 FR 60535) were considered within the context of the food supply and dietary consumption patterns. The residues of pesticidal substances that are the subject of the proposed exemption are components of a human diet. In developing the proposal, the Agency considered that the diet includes all of the food items that are customarily eaten by human populations or subpopulations. The consumption of food plants is part of a balanced and varied diet. Individuals recognize and are familiar with the plant crop derived food they consume and, based on prior experience with food, individuals avoid potential exposures to foods containing substances they know, either through personal experience or through acquired knowledge, cause them problems. Since the proposed exemption will not affect the current pattern of exposure to the

pesticidal substances that are the subject of the proposed exemption, the current method whereby sensitive individuals recognize and avoid foods known to cause them problems will not be altered. As noted in the proposal (59 FR at 60505), "consumer experience with the handling and preparation of food from these plants contributes to the safety of food from these plants.

The approach used by EPA to evaluate the dietary risk posed by the pesticidal substance component of plant-pesticides derived from sexually compatible plants (59 FR 60535) differs somewhat from the approach the Agency uses for other pesticides. For more traditional pesticides, EPA's risk evaluation relies on, for the most part, data generated by testing in laboratories using representative, single species animal model systems to estimate risk end-points such as toxicity and carcinogenicity. Conclusions from data generated from these single species testing systems are then extrapolated to conclusions concerning hazards to humans, including conclusions on dietary hazards presented by chemical pesticide residues in crops and domestic animals used as food sources for humans. Mathematical models, as well as experimental data, on pesticide residues, provide information on exposure. Exposure and hazard considerations are combined to quantify the potential risk associated with a traditional pesticide. Safety factors are often used in the risk assessment as an added measure of caution when toxicity data from surrogate animal testing are used to estimate human toxicity. Such safety factors are not necessary in risk assessment when data on human effects is directly available, as is the case for the proposed exemption from the requirement of a tolerance for residues of pesticidal substances derived from sexually compatible plants.

The approach to assessing risk described in the preceding paragraph is appropriate for analyzing risks posed by pesticide residues from pesticides such as chemical pesticides, pesticides extracted from plants, and some types of non-exempt plant-pesticides. For example, some chemicals used as pesticides may have no history of safe dietary consumption because they were created by humans and are synthetic. Single species animal testing may provide the only data on the effect of these pesticides on living organisms. Chemical pesticides that do not occur in nature, but are a product of human intervention, may not necessarily be subject to the processes by which biotic substances are degraded or cycled in nature. Thus, they may persist in the

environment for long periods of time and may bioaccumulate in the tissues of living organisms.

The risk assessment methodology appropriate for such chemicals is not appropriate for the pesticidal substances that evolved in the plant and are the subject of the proposed exemption (59 FR 60535). Plant-pesticides derived from sexually compatible plants differ from more traditional pesticides in a number of ways. As noted in the proposal (59 FR at 60511), the major characteristic of plant-pesticides that is different from traditional pesticides is that the plant itself produces the pesticidal substance rather than the pesticide being applied to the plant. Thus, the exposure pattern may be very different for plant-pesticides than for traditional pesticides both because of how the pesticide is produced and the biology of plants. . . . the potential for causing adverse health effects may be more circumscribed than for traditional pesticides because, in many cases, the only significant route of human exposure may be oral." Several conditions limit the potential for exposure to plant-pesticides as compared to traditional pesticides. These include that: (1) Exposure with plant-pesticides would be primarily through one route (dietary), (2) production of the pesticidal substance is limited by the plant's physiological constraints, (3) plant-pesticides derived from sexually compatible plants are integral parts of a plant's metabolism and thus are compatible with the biological processes of other organisms. Because of their biotic nature, the pesticidal substances that are the subject of the proposed exemption do not persist in the environment nor do they bioaccumulate in the tissues of living organisms. Thus, the number of routes of exposure that must be considered in performing a risk assessment are reduced since the primary route of exposure to plant-pesticides will be ingestion of plant tissues that contain the pesticidal substances that are the subject of the proposed exemption.

When EPA proposed to exempt residues of pesticidal substances derived from sexually compatible plants from the requirement of a tolerance (59 FR 60535), it considered health risks to the general population, which included infants and children. Children and infants, like adults, have been consuming food containing the pesticidal substances that are the subject of the proposed exemption. There is no evidence such pesticidal substances, as a component of food, present a different level of dietary risk for infants and children than they would for the adult

population. EPA's risk assessment in the proposed exemption included subgroups as part of the general population, (i.e., infants and children and the effects of culture on diet), and allowed for consumption pattern differences of such subgroups. For infants and children and other subgroups, EPA relied on the human experience base that it describes in summary form in this supplemental notice. On the basis of its analysis, EPA determined that a tolerance would not be necessary to protect the health of infants and children because pesticidal substances derived from sexually compatible plants would not pose significant new dietary exposures and experience indicates that plant-pesticides that are the subject of the exemption present no hazard under the use conditions.

### *B. Risk Assessment in Light of Amendment to FFDCFA*

After EPA issued its proposed exemption from the requirement of a tolerance for plant-pesticides derived from sexually compatible plants (59 FR 60535), Congress enacted FQPA and amended certain FFDCFA provisions governing pesticide chemical residues and FIFRA provisions governing pesticides (See Unit II. of this supplemental notice). Congress revised the specific wording of the section 408 standard for exemptions and provided more specific guidance regarding some of the factors that EPA should consider in establishing such exemptions (see Unit II. of this supplemental notice). When EPA proposed the exemption for residues of pesticidal substances derived from sexually compatible plants (59 FR 60535), it considered most of the safety factors spelled out in FQPA even though the Agency may not have explicitly discussed all those factors using the terminology specified in the FQPA amendments. This supplemental notice describes how the Agency took account of most of the FQPA factors in issuing its 1994 proposal to exempt pesticidal substances derived from sexually compatible plants and indicates which factors were considered in that proposal. The information the Agency relied on in considering these factors is part of the public record which was available to the public when EPA issued the proposed exemption from the requirement of a food tolerance. The supplemental notice also identifies the factors that were not considered in the proposal. Because FQPA amended FIFRA by incorporating the section 408 safety standard, commenters should be aware that comments on this supplemental notice

may also affect EPA's final determination on the proposed exemption (59 FR 60519) under FIFRA for plant-pesticides that are derived from plants sexually compatible with the recipient plant.

1. *Validity, completeness, and reliability of available data.* EPA considered in 1994 the validity, completeness, and reliability of the available data with regard to pesticidal substances derived from sexually compatible plants in the proposals (59 FR 60519 and 60535) and has summarized the evaluation in Unit IV.A. of this supplemental notice.

2. *Nature of toxic effect.* EPA in 1994 considered the nature of the toxic effects caused by pesticidal substances derived from sexually compatible plants in the proposals (59 FR 60519 and 60535) and has summarized its evaluation in Unit IV.A. of this supplemental notice.

3. *Relationship of studies to humans.* EPA in 1994 considered the available information concerning the relationship to humans of toxic effects of pesticidal substances that are the subject of the proposed exemption when it issued the proposals (59 FR 60519 and 60535) and has summarized that evaluation in Unit IV.A. of this supplemental notice. EPA based its evaluation on the history of human consumption of food derived from crop plants, and from products such as meat and milk from animals that consume forage and other crops (e.g., corn and other grains) that contain residues of pesticidal substances that are the subject of the proposed exemption (59 FR 60535). Because knowledge of human consumption of food derived from sexually compatible plants was available and adequately addressed the issues of hazard and exposure, the Agency did not use, for the proposed exemption (59 FR 60535), data generated in the laboratory through animal testing.

4. *Dietary consumption patterns.* EPA considered in the 1994 proposal (59 FR 60535) the available information on the varying dietary consumption patterns of major identifiable consumer subgroups as it pertains to pesticidal substances derived from sexually compatible plants. The Agency's evaluation is summarized in Unit IV.A. of this supplemental notice.

5. *Available information concerning cumulative effects of the pesticide chemical residue and other substances that have a common mechanism of toxicity.* In the 1994 proposal (59 FR 60535), EPA examined available information on the cumulative effect of pesticidal substances derived from sexually compatible plants as well as other substances present in food that

may have a common mechanism of toxicity with such pesticidal substances. EPA summarizes this information and its analysis in Unit IV.A. of this supplemental notice.

With regard to the pesticidal substance itself, the proposal notes (59 FR at 60505) that this exemption "is based upon the premise that new dietary exposures would not likely arise for plant-pesticides produced in food plants if the genetic material leading to the production of the plant-pesticide is derived from sexually compatible plants." Thus, the proposal would exempt residues of pesticidal substances that are normally components of (not new to) food from plants in sexually compatible populations. As discussed in Unit IV.A. of this supplemental notice, differences in the levels of pesticidal substances present may occur between plants in a sexually compatible population. EPA determined in the proposals that changes in the levels of these pesticidal substances are not likely to result in overall significantly different dietary exposures. As noted in the proposal (59 FR at 60538)

"[e]xtensive use and experience show the safety of foods containing these substances." If, however, information becomes available that indicates this finding is no longer consistent with the FFDCFA exemption standard for a pesticidal substance in this category, EPA will consider the validity of the new information and act to amend this tolerance exemption as necessary to protect the public health. In the 1994 proposal (59 FR at 60535), EPA is proposing a requirement that any person who sells or distributes plant-pesticides that have been exempted must report to EPA any information that comes into their possession regarding unreasonable adverse effects of an exempted plant-pesticide on human health or the environment.

With regard to substances in food that may share a common mechanism of toxicity with the residues of the pesticidal substances that are the subject of the proposed exemption (59 FR 60535), EPA considered the effects of these substances when it addressed the safety of food. Food from plants has thousands of constituents. Thus, EPA cannot rule out the possibility that the foods humans consume would also contain substances that have a common mechanism of action with the pesticidal substances that are the subject of the proposed exemption. However, because sexually compatible plants share a common pool of genetic material, any substances that may share a common mechanism of toxicity with the subject

of the proposed exemption (59 FR 60535) are normally components of (not new to) food from plants in sexually compatible populations. As discussed in the 1994 preamble and supporting record for the proposal, food from plants in sexually compatible populations have historically been safely consumed by humans either directly, or indirectly in products such as meat and milk that are derived from animals that consume forage and other crops (e.g., corn and other grains). The history of safe consumption indicates that any cumulative effects between substances in food that may have a common mechanism of toxicity with the pesticidal substances that are the subject of the proposed exemption present a very low probability of human risk. The analysis made in the preceding paragraph concerning potential increases in levels of pesticidal substances apply equally to constituents of food that may have a common mechanism of action with the pesticidal substances that are the subject of this exemption (59 FR 60535). Variation in the levels of these substances are not likely to result in overall significantly different dietary exposures. As noted in the proposal (59 FR at 60538) "plant varieties that meet the sexually compatible standard produce food that is safe for human consumption and/or appropriate processing procedures are widely known and routinely used by consumers in preparation of food from such sources." However, should EPA in the future identify substances with a common mechanism of toxicity with the plant-pesticides that are the subject of the proposed exemption, both FIFRA and FFDCA give the Agency adequate authority to take appropriate action to address any risks to humans health.

EPA is not aware of any other substances outside of the food supply that may have a common mechanism of toxicity with the residues of the pesticidal substances that are the subject of the proposed exemption (59 FR 60535), although it cannot rule out the possibility. Should EPA in the future identify substances with a common mechanism of toxicity other than those found in the parts of plants used as food, both FIFRA and FFDCA give the Agency adequate authority to take appropriate action to address any risks to humans health.

Because EPA already considered the safety of food containing residues of pesticidal substances derived from sexually compatible plants and other constituents of food that may share a common mechanism of toxicity with those residues when it issued the proposal (FR 60535), it is not requesting

additional comment on that topic. Comments are requested only on the new issue of whether there are any substances outside of the food supply that have a common mechanism of toxicity with the residues of the pesticidal substances that are the subject of the proposed exemption, and the effects of any such substances on human health.

6. *Aggregate exposures of consumers including non-occupational exposures.* EPA considered the available information on the aggregate exposure level of consumers to pesticidal substances in the plant-pesticides to be exempt in the 1994 FFDCA and FIFRA proposals (59 FR 60519 and 60535). This included a consideration of exposures from dietary sources (59 FR 60535) as well as from other non-occupational sources (59 FR 60519). As indicated in EPA's policy statement, "plant-pesticides are likely to present a limited exposure of the pesticidal substance to humans. In most cases, the predominant, if not the only, exposure route will be dietary. Significant respiratory and dermal exposures will be unlikely" (59 FR at 60513). As explained in the FFDCA and FIFRA proposals and the EPA's policy statement (59 FR 60494) and associated dockets, plant-pesticides present negligible exposure of pesticidal substances to humans outside of the dietary route because the substances are in the plant tissue and thus are found either within the plant or in close proximity to the plant. EPA considered dietary exposure to the pesticidal substances in the proposed FFDCA exemption (59 FR 60535) and summarized its evaluation in Unit IV.A. of this supplemental notice.

Despite EPA's belief that, because of the nature of plant-pesticides, there is little likelihood of exposure other than through the dietary route, EPA in this supplemental notice sets forth in greater detail its considerations concerning other exposure routes. With regard to the dermal route of exposure, the pesticidal substances that are the subject of the proposed exemption (59 FR 60535) may in some cases be present in sap or other exudates from the plant or the food 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. Individuals preparing meals are those most likely to experience dermal contact with the substances on a non-occupational basis. However, on a per person basis, the potential amounts involved in these exposures are negligible in comparison to potential

exposure through the dietary route. Moreover, substances that occur naturally in food, including the pesticidal substances that are the subject of the proposed exemption, are unlikely to cross the barrier provided by the skin and thus the responses seen on rare occasions to substances in food are most likely to be localized skin irritations. Whether these irritations are caused by the pesticidal substance component of plant-pesticides is unknown but given the thousands of constituents of any food of plant origin, the probability that substances other than the plant-pesticides are the irritants is very high. Because substances present in food are unlikely to pass through the skin, dermal exposures are not additive to dietary exposures.

With regard to exposure through inhalation, the pesticidal substances may in some cases be present in pollen and some individuals (those near enough to farms, nurseries or other plant-growing areas to be exposed to wind-blown pollen) may be exposed, through inhalation, to the pollen. On a per person basis, the potential amounts of pollen involved in these exposures are negligible in comparison to potential exposure through the dietary route. Moreover, it is unlikely that exposure to the pollen is equivalent to exposure to the pesticidal substance. The pesticidal substance will not in every case be present in the pollen. When it is present in pollen, the pesticidal substance will be integrated into the tissue of the pollen grain. EPA cannot rule out the possibility that in some cases, the pesticidal substance or some piece of the pesticidal substance might be bound to the surface of the pollen grain (as opposed to the more likely circumstance of the substance being within the pollen grain). If the substance is bound to the surface of the pollen, lung or respiratory tract tissue in humans might be exposed to the pesticidal substance. Substances that occur naturally in pollen, including the pesticidal substances that are the subject of the proposed exemption, are unlikely to cross the barrier provided by the mucous membrane of the respiratory tract and thus are not additive to dietary exposure.

EPA also evaluated potential non-occupational exposures in drinking water. As noted in the preceding paragraphs, the substances in plants or parts of plants, including the pesticidal substances that are the subject of the proposed exemption (59 FR 60535), are produced inside the plant itself. The pesticidal substances are integrated into and an integral part of the living tissue of the plant. When the plant dies or a part is removed from the plant,

microorganisms colonizing the tissue immediately begin to digest it, using the components of the tissue (including any pesticidal substances in the tissue) as building blocks for making their own tissues or for fueling their own metabolisms. The pesticidal substances that EPA proposed to exempt are subject to the same processes of degradation and decay that all organic matter undergoes. This turnover of biochemical materials in nature through a process of degradation occurs fairly rapidly. Therefore, these pesticidal substances do not persist in the environment or bioaccumulate. There is no indication that naturally occurring plant biochemical compounds, including the pesticidal substances that are the subject of the proposed exemption, are resistant to this degradation. Because of the fairly rapid turnover of these substances, even if they reach surface waters (through pollen dispersal or parts of the plants (leaves, fruits etc.) falling into bodies of water), they are unlikely to present anything other than a negligible exposure in drinking water drawn from surface water sources. Should they resist degradation long enough to enter groundwater, they are unlikely to present anything other than a negligible exposure in drinking water drawn from groundwater. Therefore, although a potential for non-dietary exposure (i.e., non-food oral, dermal and inhalation) in non-occupational settings may exist, EPA expects such exposure to be negligible.

With regard to exposure to "other related substances," EPA is not aware of any other substances that may be related, via a common mechanism of toxicity, to the pesticidal substances that are the subject of the proposed exemption (59 FR 60535), other than related substances that are present in parts of plants used as food. Thousands of substances are present in the edible parts of plants. These may include substances related, via a common mechanism of toxicity, to the pesticidal substances that are the subject of the proposed exemption. These related substances have long been accepted as part of the human diet. Extensive use and experience show the safety of foods containing these substances. It also shows the safety of these substances consumed in aggregate through the dietary route with the pesticidal substances that are the subject of the proposed exemption. With regard to non-occupational exposure through routes other than dietary exposure, no evidence, in the many years of human experience with the growing and consumption of food from plants that

may contain substances that may be related via a common mechanism of toxicity to the pesticidal substances that are the subject of the proposed exemption, indicates that adverse effects due to aggregate exposure through the dietary, non-food oral, dermal and inhalation routes occurs.

Should EPA in the future identify substances related via a common mechanism of toxicity to the pesticidal substances that are the subject of the proposed exemption, FIFRA and the FFDCFA provide the Agency adequate authority to take appropriate action to address any risks associated with those related substances. Substances that are isolated from the plant's tissues, concentrated and then applied topically as pesticides to the plant or to food would not be covered by the proposed exemption (59 FR 60535), but would be subject to the tolerance requirements of FFDCFA.

Because the Agency already considered exposure to the pesticidal substances that are the subject of the proposed exemption (59 FR 60535) and to substances related via a common mechanism of toxicity to these pesticidal substances in food when it issued the proposal, it is not requesting additional comment on this topic. Comments are requested only on the issue of whether there are additional substances outside that food supply that are related, via a common mechanism of toxicity, to residues of the pesticidal substances that are the subject of the proposed exemption and the effects of exposure to any such substances on human health.

*7. Sensitivities of subgroups.* In 1994, EPA considered available information on the sensitivities of subgroups as it pertains to the pesticidal substances derived from sexually compatible plants in the proposal (59 FR 60535) and has summarized the evaluation in Unit IV.A. of this supplemental notice.

*8. Naturally occurring estrogen or other endocrine effects.* FFDCFA now directs EPA, in establishing an exemption from the requirement of a tolerance, to consider "such information as the Administrator may require on whether the pesticide chemical may have an effect in humans that is similar to an effect of a naturally occurring estrogen or other endocrine effect" (21 U.S.C. 346(a)(q)). Congress allowed EPA 2 years to establish a screening program to determine whether certain pesticide chemicals may have estrogenic effects and an additional year to implement the program (21 U.S.C. 408(p)). As part of the screening and implementation process, EPA is determining what information might be required and how

it will address estrogenic effects from pesticide residues in general.

While there is some information on estrogenic effects from exposure to certain pesticides, the data are limited. It is known that certain food plants contain estrogen mimics, termed phytoestrogens. Such phytoestrogens are currently being consumed by humans in food derived from plants. EPA cannot rule out the possibility that such phytoestrogens could be used as plant-pesticides. Potential exposure of humans via consumption of plant tissue to phytoestrogens exerting estrogenic effects and used as plant-pesticides may need to be considered when the issue of endocrine disruptors is examined by EPA. If dietary exposure to phytoestrogens (that are also plant-pesticides) is discovered to be a significant factor, the Agency will re-examine this proposed exemption from the requirement of a tolerance (59 FR 60535) in light of that information.

*9. Safety factors.* In the 1994 proposal, EPA did not rely on the available animal data in reaching its determination that a tolerance is not necessary to protect the public from pesticidal substances derived from sexually compatible plants (59 FR 60535). As discussed in Unit IV.A. of this supplemental notice, EPA relied on the long history of safe human consumption of the pesticidal substances that are the subject of the proposed exemption in food from sexually compatible plant populations and in food derived from animals that consume forage and other crops (e.g., corn and other grains). EPA continues to believe that long-term evidence of human consumption, not animal experimentation data, is the appropriate information base for the proposed exemption (59 FR 60535). Because EPA did not rely on animal experimentation data, the Agency did not consider which safety factors would be appropriate to use in assessing risk to humans based on data generated through experiments on animals.

*10. Infants and children.—a. Dietary consumption patterns.* In the 1994 proposal (59 FR 60535), EPA considered available information on the dietary consumption pattern of infants and children as pertains to the pesticidal substances derived from sexually compatible plants and has summarized the evaluation in Unit IV.A. of this supplemental notice. The range of foods consumed by infants and children is in general more limited than the range of foods consumed by adults. Most newborns rely on milk products for nutrition, although some infants are fed soy based products. Infants begin as early as 4-months of age to consume

specific types of solid foods containing residues of pesticidal substances that are the subject of the proposed exemption. Subsequent to 4 months of age, apart from processing to facilitate swallowing, the diets of infants are based on foods consumed by the general adult population albeit in different proportions. As infants and children mature, more and more of the foods normally consumed by adults become part of their diets and the relative proportions of the different types of food consumed changes to more closely resemble an adult diet.

b. *Special susceptibility.* In the 1994 proposal (59 FR 60535), EPA considered available information on the potential for susceptibility of infants and children, including pre- and post-natal toxicity, as these factors pertain to the pesticidal substances derived from sexually compatible plants and has summarized the evaluation in Unit IV.A. of this supplemental notice.

c. *Cumulative effects of residues with other substances with a common mechanism of toxicity.* In the 1994 proposal (59 FR 60535), EPA examined the available information on the cumulative effect of residues of pesticidal substances derived from sexually compatible plants as well as other substances in food that may have a common mechanism of toxicity. The Agency's consideration in the proposal of the effects of the residues of pesticidal substances that are the subject of the proposed exemption (59 FR 60535) for the general population also included consideration of effects for infants and children. See Unit IV.B.5. of this supplemental notice for a discussion of cumulative effects of the pesticide chemical residues and other substances that have a common mechanism of toxicity.

Because EPA already considered the safety of food containing residues of pesticidal substances derived from sexually compatible plants and other constituents of food when it issued the proposal (FR 60535), the Agency is not requesting additional comment on that topic. Comments are requested only on the new issue of whether there are any substances outside of the food supply with a common mechanism of toxicity to the residues of the pesticidal substances that are the subject of the proposed exemption and the effects of any such substances on infants and children.

d. *Margin of safety.* In determining whether the residues of the pesticidal substances that are the subject of the proposed exemption (59 FR 60535) are safe, FFDCA section 408(b)(2)(C) directs EPA to apply a tenfold margin of safety

for the residues and other sources of exposure to infants and children to account for potential pre- and post-natal toxicity and completeness of data on threshold effects with respect to exposure and toxicity to infants and children, unless a different margin will be safe. In proposing the exemption, EPA based its assessment of exposure and toxicity upon reliable information (Ref. 1) including the long history of safe human consumption of food containing residues of the pesticidal substances that are the subject of the proposed exemption and other substances in food that may have a common mechanism of toxicity, and the unique nature of plant-pesticides. EPA did not rely on animal data. EPA relied on observations concerning whole food consumption by humans and did not rely on single entity testing, wherein substances are isolated from a plant source, and fed to animals at high concentrations (Ref. 1). EPA relied on the vast experiential base of actual food consumption patterns rather than limited testing situations. EPA thus, did not utilize animal or other studies that would yield data that could be subjected to an additional margin of safety. (See Units IV.A. and IV.B.3. of this supplemental notice). As a result, the FQPA amendments to FFDCA do not affect EPA's analysis.

#### C. Safety Determinations in Light of FFDCA Amendment

Based on the information discussed in the 1994 proposals (59 FR 60496 through 60547), the discussion in Unit IV.A. and the analysis in Unit IV.B. of this supplemental notice, EPA concludes that there is a reasonable certainty that no harm will result to the U.S. population in general, and U.S. infants and children, from aggregate exposure to residues of pesticidal substances derived from sexually compatible plants, including all anticipated dietary exposures and all other exposures for which there is reliable information. Under the proposed exemption from the requirement for a tolerance (59 FR 60535), EPA would exempt residues of pesticidal substances that are normally components of (not new to) food from plants in sexually compatible populations. Extensive use and experience show the safety of foods containing these substances. No evidence, in the many years of human experience with the growing and consumption of food from plants containing the pesticidal substances that are the subject of the proposed exemption (59 FR 60535), indicates that adverse effects due to aggregate

exposure through the dietary, non-food oral, dermal and inhalation routes occur.

The conclusion that residues of pesticidal substances derived from sexually compatible plants should be exempt from tolerance requirements under the FFDCA section 408 safety standard also lends support to EPA's proposed FIFRA exemption (59 FR 60519) for plant-pesticides derived from sexually compatible plants with respect to human dietary risks. In the FIFRA proposal, EPA utilized two criteria to determine whether plant-pesticides should be exempt: (1) Whether they posed a low probability of risk, and (2) whether they caused unreasonable adverse effects on the environment. Based upon the determination that residues of pesticidal substances subject to the proposed exemption (59 FR 60535) and the nucleic acid component of plant-pesticides (59 FR 60542) meet the FFDCA section 408 safety test, EPA concludes plant-pesticides derived from sexually compatible plants would pose only a low probability of human dietary risk and also would not pose an unreasonable adverse effect with respect to such risks.

#### D. Other Considerations

When the Agency proposed to establish an exemption from the requirement of a tolerance for residues of pesticidal substances derived from sexually compatible plants (59 FR 60535), EPA did not propose any numerical limitation on the amount of pesticidal substance that could be present in food containing these residues. EPA consulted in 1994 with the Department of Health and Human Services (DHHS) in developing the proposed exemption (59 FR 60535) and this supplemental notice and will consult with the Secretary of HHS prior to issuing the final rule. Because the 1994 proposal was for the exemption from the requirement of a tolerance, the Agency has concluded that an analytical method for detecting and measuring the levels of the residues of the subject pesticidal substances in or on food is not required.

#### V. Comments

##### A. Confidential Business Information

Information submitted as comments concerning this supplemental notice may be claimed confidential by marking any part or all of that information as "Confidential Business Information" (CBI). CBI should not be submitted through e-mail. Information marked as CBI will not be disclosed except in accordance with procedures set forth in

40 CFR part 2. A copy of the comment that does not contain CBI must be submitted for inclusion in the public record. Information not marked confidential may be disclosed publicly by EPA without prior notice.

#### B. 30-Day Comment Period

EPA is allowing a 30-day comment period because it has determined that such a period will provide the public with an adequate opportunity to respond to the additional issues raised in this supplemental notice. FFDCA and FIFRA do not specify a comment period for this type of notice. EPA has decided that a 30-day comment period is reasonable because this supplemental notice raises very few new issues that were not already available for public comment. As discussed in Unit IV. of this supplemental notice, EPA effectively considered most of the factors required by the FQPA amendments of FFDCA and FIFRA relevant to the proposed exemptions when it issued the proposed package of notices describing EPA's approach in 1994 (59 FR 60496, 60519, 60535, 60542 and 60545). At that time, the public had an opportunity to review both the Agency's rationale for the proposals and the underlying support documents during a 90-day public comment period. Only a limited number of new issues have been raised by the FQPA amendments to FFDCA and FIFRA and the Agency continues to rely upon the information already in the docket for the 1994 proposals and thus 30 days should provide adequate time for public comment. In addition, EPA believes that it is in the interest of the public to publish the final exemption from the requirement of a tolerance in a timely manner.

#### C. Request for Comments

Interested persons are invited to submit written comments on the new issues raised in this supplemental notice specifically on:

(1) Whether there are substances, outside of the food supply, sharing a common mechanism of toxicity with pesticidal substances that are derived from sexually compatible plants. Commenters are asked to submit information on the cumulative effects of such substances and the pesticidal substances that are the subject of the proposed exemption (59 FR 60535).

(2) Whether there are substances, outside of the food supply, related via a common mechanism of toxicity to pesticidal substances that are derived from sexually compatible plants, to which humans might be exposed through non-occupational routes of

exposure. Commenters are asked to describe routes through which such exposure might occur, including exposure to major identifiable subgroups of human populations (e.g., infants and children). If such routes are identified, commenters are requested to provide information on the nature and levels of the expected exposure.

Entities may also offer comments on issues V.C.1. and V.C.2. above as they apply to Option 2 as described in the November 23, 1994 **Federal Register** (59 FR at 60537) "Plant-pesticides derived from plants within the same genus or from sexually compatible plants" under the revised FFDCA section 408 safety standard. The Agency will not consider comments that address issues or information already presented for public comment in the proposed rule issued in the November 23, 1994, **Federal Register**.

Commenters who possess information on substances occurring in food that may have estrogenic effects and may be used as plant-pesticides are requested to send such information to EPA.

In this supplemental notice, EPA describes in greater detail the rationale supporting the statement made in the 1994 **Federal Register** (59 FR at 60513) that "plant-pesticides are likely to present a limited exposure of pesticidal substances to humans. In most cases, the predominant, if not the only route of exposure will be dietary. Significant respiratory and dermal exposures will be unlikely." No comments were received on this statement during the official comment period. Commenters may comment on this more detailed rationale.

In this supplemental notice, EPA also describes in greater detail how the rationale presented in the 1994 **Federal Register** (59 FR at 60538) concerning the safety for human consumption of food from plants that meet the sexually compatible standard applies to infants and children. No comments were received on this statement during the official comment period. Commenters may comment on this more detailed rationale specifically addressing infants and children as part of the larger human population.

#### VI. Public Docket

The official record for this rulemaking, as well as the public version, has been established for this rulemaking under docket control number "OPP-300368A" (including comments and data submitted electronically as described below). A public version of this record, including printed, paper versions of electronic comments, which does not include any

information claimed as CBI, is available for inspection from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The official rulemaking record is located at the address in "ADDRESSES" at the beginning of this document.

Electronic comments can be sent directly to EPA at:

opp-docket@epamail.epa.gov  
Electronic comments must be submitted as an ASCII file avoiding the use of special characters and any form of encryption. Comment and data will also be accepted on disks in Wordperfect 5.1 file format or ASCII file format. All comments and data in electronic form must be identified by the docket control number "OPP-300368A." Electronic comments on this supplemental notice may be filed online at many Federal Depository Libraries.

#### VII. References

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

#### VIII. Regulatory Assessment Requirements

This supplemental notice merely seeks additional comments on the proposed rules with regard to the potential impact that the new statutory amendments imposed by the August 3, 1996 Food Quality Protection Act (FQPA) might have on the provisions as proposed. As such, this notice does not contain any new proposed requirements that would require additional consideration by the Office of Management and Budget (OMB) under Executive Order 12866, entitled Regulatory Planning and Review (58 FR 51735, October 4, 1993) or the Paperwork Reduction Act (PRA), 44 U.S.C. 3501 *et seq.* It does not require any other action under Executive Order 12875, entitled Enhancing the Intergovernmental Partnership (58 FR 58093, October 28, 1993), Executive Order 12898, entitled Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations (59 FR 7629, February 16, 1994), or the Regulatory Flexibility Act (RFA) (5 U.S.C. 601 *et seq.*). The Agency's activities related to these regulatory assessment requirements are discussed in the proposed rules.

EPA did not consider Title II of the Unfunded Mandates Reform Act of 1995 (UMRA) (Pub. L. 104-4) at the proposal stage because the proposed rules were

issued prior to its enactment. Although this supplemental notice is not subject to UMRA because it neither proposes or finalizes any regulatory requirements, the applicability of the UMRA requirements will be addressed in the final rules.

#### List of Subjects in 40 CFR Part 180

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides and pests, Plants, Plant-pesticides, Reporting and recordkeeping requirements.

Dated: May 7, 1997.

**Lynn R. Goldman**

*Assistant Administrator for Prevention, Pesticides and Toxic Substances.*

[FR Doc. 97-12784 Filed 5-15-97; 8:45 am]

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## ENVIRONMENTAL PROTECTION AGENCY

### 40 CFR Part 180

[OPP-300371A; FRL-5716-7]

RIN 2070-AC02

#### Plant-Pesticides; Nucleic Acids; Supplemental Notice of Proposed Rulemaking

**AGENCY:** Environmental Protection Agency (EPA).

**ACTION:** Supplemental notice of proposed rulemaking.

**SUMMARY:** This document announces the availability of information for additional public comment regarding a proposed exemption from the requirement of a tolerance under the Federal Food, Drug, and Cosmetic Act (FFDCA) for residues of nucleic acids (i.e., deoxyribonucleic acid and ribonucleic acid) produced in plants as part of a plant-pesticide. Comments on this document may also affect EPA's final determination on three proposed exemptions under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). In 1994, EPA proposed to exempt from the requirement of tolerance residues of nucleic acids produced in plants as part of a plant-pesticide because such a tolerance would not be necessary to protect the public health. Since publication of the proposal, Congress enacted the Food Quality Protection Act (FQPA) which amended FFDCA and FIFRA. EPA is issuing this document today 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 exemption from

the requirement of a tolerance for residues of nucleic acids produced in plants as part of a plant-pesticide. EPA believes that it considered most of the substantive issues associated with the FQPA amendments when it issued the proposal in 1994. EPA is, thus, in this document, specifically seeking comment only on its evaluation of the requirements imposed by FQPA that the Agency did not address in the proposal.

**DATES:** Comments, identified by the docket control number "OPP-300371A," must be received on or before June 16, 1997.

**ADDRESSES:** By mail, submit written comments to: Public Information and Records Integrity Branch, Information Resources and Services Division (7506C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. In person deliver comments to: Rm. 1132, Crystal Mall #2, 1921 Jefferson Davis Highway, Arlington, VA 22202.

Comments and data may also be submitted electronically by following the instructions under Unit VI. of this document. No Confidential Business Information (CBI) should be submitted through e-mail.

**FOR FURTHER INFORMATION CONTACT:** Elizabeth Milewski, Office of Science, Coordination and Policy, Office of Prevention, Pesticides and Toxic Substances (7101), Environmental Protection Agency, 401 M St., SW., Washington, DC 20460, Telephone: (202) 260-6900, e-mail: milewski.elizabeth@epamail.epa.gov.

#### SUPPLEMENTARY INFORMATION:

##### I. Introduction

EPA issued in the November 23, 1994 **Federal Register** a package of five separate **Federal Register** proposals (59 FR 60496, 60519, 60535, 60542 and 60545) (FRL-4755-2, FRL-4755-3, FRL-4758-8, FRL-4755-5, and FRL-4755-4) which together described EPA's approach to substances produced in plants that enable the plants to resist pests or disease. EPA's package of proposals indicated that these substances are pesticides under section 2 of FIFRA (7 U.S.C. 136(u)) if they are "intended for preventing, destroying, repelling, or mitigating any pest" or if they are ". . . intended for use as a plant regulator, defoliant, or desiccant" regardless of whether the pesticidal capabilities evolved in the plants or were introduced by breeding or through the techniques of modern biotechnology. These substances, and the genetic material necessary to produce them, were designated "plant-pesticides" by EPA in the November 23,

1994, **Federal Register** notices. The notices defined a "plant-pesticide" as "a pesticidal substance that is produced in a living plant and the genetic material necessary for the production of the pesticidal substance where the pesticidal substance is intended for use in the living plant" (59 FR at 60534).

One of the five documents (59 FR 60542) proposed to exempt from the requirement of a tolerance residues of nucleic acids (i.e., deoxyribonucleic acid (DNA) and ribonucleic acid (RNA)) when such nucleic acids are produced in plants as part of a plant-pesticide (i.e., the genetic material necessary to produce the pesticidal substance). This supplemental notice addresses the nucleic acids portion of plant-pesticides produced in food plants. Because FQPA modified FIFRA (7 U.S.C. 136 *et seq.*) by incorporating the FFDCA safety standard into the FIFRA test for determining whether a pesticide poses an unreasonable adverse effect, comments on this supplemental notice may also affect EPA's final determination on proposed exemptions under FIFRA for three categories of plant-pesticides (59 FR at 60535): (1) Those that are derived from a plant that is sexually compatible with the recipient plant, (2) those that act primarily by affecting the plant, and (3) those that are coat proteins from plant viruses.

EPA is publishing this supplemental notice to ensure that the public has had adequate opportunity to comment on certain new considerations raised by the FQPA amendments to FFDCA as these considerations relate to the proposed exemption from a tolerance for residues of the nucleic acid portion of plant-pesticides produced in food plants. In evaluating a pesticide chemical residue for exemption from FFDCA tolerance requirements, EPA must now explicitly address certain factors, and make a determination that there is a reasonable certainty that aggregate exposure to the residue will cause no harm to the public. The factors to be considered are iterated in Unit II. of this supplemental notice. EPA's evaluation of these factors relative to the proposed exemption (59 FR 60535) is contained in Unit IV. of this supplemental notice. Consistent with FFDCA section 408(c)(2)(B), EPA has reviewed the available scientific data and other relevant information in support of this action. In today's supplemental notice, EPA requests comment only on the new conclusions identified in Unit V.C.

In light of FQPA, EPA is engaged in a process, including consultation with registrants, states, and other interested stakeholders, to make decisions on the