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.

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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

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 residues of nucleic acids produced in plants as part of a plant-pesticide, 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 chemical pesticide 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 Regulation

The proposal (59 FR 60542) described how EPA would view: (1) Deoxyribonucleic acid (DNA) and ribonucleic acid (RNA), (2) nucleic acid analogues (e.g., altered purine or pyrimidine bases) that may be considered ''nucleic acids'' by their chemical composition, and (3) DNA sequences that code for the RNA complement (anti-sense) of the messenger RNA (mRNA) for an essential enzyme or other component of an obligate parasite.

In the November 23, 1994 **Federal Register**, EPA proposed to exempt nucleic acids (i.e., deoxyribonucleic acid (DNA) and ribonucleic acid (RNA)) from the requirement of a tolerance when such nucleic acids are produced in plants as part of a plant-pesticide (59 FR 60542). In the proposal, EPA stated that the proposed exemption from the requirement of a tolerance for the nucleic acids portion of plant-pesticides produced in food plants is based on the ubiquity of nucleic acids in all forms of life, their presence in human and domestic animal food and the consequent large scale exposure of the human population with no evidence nucleic acids have caused any adverse health effects when consumed as part of a food plant. The Agency knows of no instance where nucleic acids naturally occurring in plants have been associated with any toxic effects related to the consumption of foods.

In the 1994 proposal, EPA recognized that nucleic acid analogues (e.g., altered purine or pyrimidine bases) may be considered ''nucleic acids'' by their chemical composition. Certain analogues are being developed as therapeutic agents for human diseases and nucleic acid analogues could conceivably be developed as pesticides. The proposed exemption does not extend to such nucleic acid analogues. The 1994 proposal only proposed to exempt the naturally occurring, non-modified nucleic acids (ribosides or deoxyribosides of A, T, G, C, and U) and polymers of such substances commonly found in living cells that encode the information necessary to make the pesticidal substances produced by plants.

The 1994 proposal also discussed how EPA proposed to view the introduction into plants of DNA sequences that code for the RNA complement (anti-sense) of the messenger RNA (mRNA) for an essential enzyme or component of an obligate parasite. One mechanism by which this RNA complement or anti-sense RNA is believed to work is to bind to the target mRNA and prevent it from binding to ribosomes, effectively terminating synthesis of the essential enzyme or other enzymes for making other essential cellular components necessary to survival of the parasite. This methodology is currently being developed for introducing pest-resistance into plants. As was noted in the proposed exemption, the Agency believes that the introduction and expression in plants of nucleic acids in this anti-sense technology do not present a hazard to the public health and such nucleic acids would qualify for this food tolerance exemption.

IV. Risk Assessment and Safety Determinations

A. Risk Assessment in Proposal

This unit reviews the analysis that EPA used to support its 1994 proposal (59 FR 60535) to exempt nucleic acids (DNA and RNA, including DNA and RNA used in anti-sense technology) produced in plants as part of a plant-pesticide from the requirement of a tolerance under 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 three categories of plant-pesticides (59 FR at 60535) from most FIFRA requirements. Non-dietary human risks from exposure to nucleic acids as part of plant-pesticides 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.

EPA's 1994 proposal (59 FR 60542) to exempt nucleic acids produced in plants as part of a plant-pesticide from the requirement of a tolerance was based on the ubiquity of nucleic acids and their presence in human and domestic animal food without observed adverse health effects.

Nucleic acids encode the information necessary for the functioning of the organism. Chemically, nucleic acids occur in two types: deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). DNA and RNA can be thought of as a ''tape'' containing information. DNA and RNA are polymers composed of small units, called ''nucleotides.'' A nucleotide is made up of a sugar, a phosphate group, and one of four heterocyclic bases. The heterocyclic bases in DNA are adenine, thymine, cytosine, and guanine. The heterocyclic bases in RNA are adenine, uracil, cytosine and guanine. The sugars and phosphates form a long chain or ''backbone'' with one heterocyclic base attached to each sugar. The information encoded in the nucleic acid is determined by the sequence in which the heterocyclic bases are attached to the sugar-phosphate backbone. Thus, the ''genetic material necessary for the production of the pesticidal substance'' are the nucleic acids encoding the information necessary for a plant cell to make the pesticidal substance.

Nucleic acids are also the chemical basis for heritable traits. When nucleic acids encoding the genetic information needed for the production of a pesticidal substance is stably integrated into the plant, that plant and its progeny will have the potential to produce the pesticidal substance.

Nucleic acids are widespread in foods and have not, by themselves, been associated with toxic or pathogenic effects on animals or humans. None of the constituents of nucleic acids are known to be acute toxicants, but like proteins and other normal constituents of food, may cause indirect, adverse metabolic effects if consumed exclusively at high doses over a long period of time in the absence of a normal balanced diet. Nucleic acids never occur at these high amounts in food plants and have not been associated with any toxic effects related to consumption of foods.

In the proposal, the Agency made clear that it is not proposing to exempt nucleic acid analogues from the requirement of a food tolerance. These analogues are not naturally occurring and those used as therapeutic agents frequently have significant toxicity associated with their use. The intent of EPA's 1994 proposal was to exempt only the naturally occurring, non-modified nucleic acids, and polymers of such substances, commonly found in living cells that serve as the mechanisms of encoding traits associated with pesticidal substances produced by plants.

EPA proposed to extend this exemption (59 FR 60542) from the requirement of a tolerance to the mRNA used in anti-sense technology based on the consideration that these mRNAs are analogous to naturally occurring, non-modified nucleic acid polymers commonly found in living cells. The rationale applied in the proposal to other naturally occurring, non-modified nucleic acid polymers applies equally to these mRNAs; the ubiquity of nucleic acids and their presence in human and domestic animal food and no observed adverse health effects associated with consumption of foods containing nucleic acids.

B. Risk Assessment in Light of Amendment to FFDCA

After EPA issued its proposed exemption from the requirement of a tolerance for nucleic acids produced in plants as part of a plant-pesticide (59 FR 60542), Congress enacted FQPA and amended certain FFDCA 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 nucleic acids produced in plants as part of a plant-pesticide (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 from the requirement of a tolerance nucleic acids produced in plants as part of a plant-pesticide, 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 exemptions (59 FR at 60535) under FIFRA for three categories of plant-pesticides: (1) Those that are derived from plants 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.

1. *Validity, completeness, and reliability of available data.* EPA considered in 1994 the validity, completeness, and reliability of the available data with regard to nucleic acids produced in plants as part of a plant-pesticide in the proposals (59 FR 60519 and 60542) and has described 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 nucleic acids produced in plants as part of a plant-pesticide in the proposals (59 FR 60519 and 60542) and has described 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 of available data on toxicity of nucleic acids produced in plants as part of a plant-pesticide to humans when it issued the proposal to exempt these substances from the requirement of a tolerance. EPA has summarized its evaluation in Unit IV.A. of this supplemental notice. The nature of the toxic effect of nucleic acids was assessed in light of the known presence of nucleic acids in all consumed foods (Ref. 1) and 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 nucleic acids. EPA determined in the proposal that nucleic acids produced in plants as part of a plant-pesticide do not have a toxic effect and have no adverse effects to humans. Because knowledge of human consumption of food containing nucleic acids was available and adequately addressed the issues of hazard and exposure, the Agency did not use, for the proposed exemption (59 FR 60542), data generated in the laboratory through animal testing.

4. *Dietary consumption patterns.* EPA considered in the 1994 proposal the available information on the varying dietary consumption patterns of major identifiable consumer subgroups as it pertains to nucleic acids in food from plants. As described in the 1994 proposal, nucleic acids are ubiquitous in nature and in the food supply. Nucleic acids that make up the genetic material in plant-pesticides will not alter this baseline consumption pattern of nucleic acids. 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.* EPA in 1994 examined the available information on the cumulative effect of nucleic acids in food from plants and other substances that have a common mechanism of toxicity. EPA summarizes this information and its analysis in Unit IV.A. of this supplemental notice.

Nucleic acids are widespread in food and have not been associated with direct toxic or pathogenic effects to animals or humans. Because nucleic acids in foods have no human toxicity, no cumulative effects can be identified for nucleic acids produced in plants as part of a plant-pesticide. FQPA also directs the Agency to examine whether there are other substances that have a common mechanism of toxicity with nucleic acids produced in plants as part of a plant-pesticide. Based on available information which indicates that nucleic acids in food have no human toxicity, EPA is not aware of any other substances that might have a common mechanism of human toxicity with nucleic acids produced in plants as part of a plant-pesticide.

EPA is not aware of any substances outside of the food supply that may have a common mechanism of toxicity with nucleic acids produced in plants as part of a plant-pesticide since nucleic acids in plant food are not toxic. EPA has identified nucleic acid analogues as substances having some level of toxicity; however, their mechanism of toxicity is not cumulative with that of naturally occurring nucleic acids (DNA and RNA).

EPA considered the safety of foods containing residues of nucleic acids when it issued the proposal and is not requesting additional comment on that topic. Comments are only requested on EPA's conclusion that there are no substances outside of the food supply that may have a cumulative toxic effect with residues of nucleic acids produced in plants as part of a plant-pesticide.

6. *Aggregate exposures of consumers including non-occupational exposures.* EPA considered the available information on the aggregate exposure level of consumers to nucleic acids produced in plants as part of a plant-pesticide in the 1994 FFDCA and FIFRA proposals (59 FR 60519 and 60542). This included a consideration of exposures from dietary sources (59 FR 60542) 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 EPA's policy statement (59 FR 60496) 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. This is particularly true for the nucleic acid portion of plant-pesticides. EPA considered dietary exposure to nucleic acids produced in plants as part of a plant-pesticide in the proposed FFDCA exemption (59 FR 60542) and summarized its evaluation in Unit IV.A. of this supplemental notice.

Despite EPA's belief that, because of the nature of nucleic acids produced in plants as part of a plant-pesticide, 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, nucleic acids produced in plants as part of a plant-pesticide 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 nucleic acids produced in plants as part of plant-pesticides, are unlikely to cross the barrier provided by the skin. This is particularly true for nucleic acids produced in plants as part of a plant-pesticide as they are large polymers.

With regard to exposure through inhalation, nucleic acids produced in plants as part of a plant-pesticide 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 nucleic acids produced in plants as part of a plant-pesticide. In pollen, nucleic acids will likely be integrated into the tissue of the pollen grain and not bound to the surface of the pollen grain. Pollen grains and the substances that occur naturally in pollen 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 nucleic acids produced in plants as part of a plant-pesticide, are produced inside the plant itself. Nucleic acids are 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 nucleic acids produced in plants as part of plant-pesticides) as building blocks for making their own tissues or for fueling their own metabolisms. Nucleic acids produced in plants as part of a plant-pesticide 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. Indeed, nucleic acids are highly unstable outside of the cellular environment and are very quickly broken down. Therefore, nucleic acids produced in plants as part of a plant-pesticide do not persist in the environment or bioaccumulate. There is no indication that naturally occurring nucleic acids produced in plants as part of plant-pesticides, are resistant to this degradation. Because of the very rapid turnover of these substances, even if they reach surface waters (e.g., through plant parts falling into bodies of water), they are unlikely to present anything other than a very negligible exposure in drinking water drawn either from surface or ground water sources. Therefore, the potential for non-dietary exposure (i.e., non-food oral, dermal and inhalation) in non-occupational settings is extremely limited and EPA expects such exposure to be negligible.

With regard to exposure to ''other related substances,'' EPA is not aware of any other substances either in food or outside the food supply that may be related, via a common mechanism of toxicity, to nucleic acids produced in plants as part of a plant-pesticide since nucleic acids are not toxic. With regard to non-occupational exposure through routes other than dietary exposure, since nucleic acids have no mechanism of toxicity, EPA is not aware of substances in food or outside the food supply that may be related via a common mechanism of toxicity to the nucleic acids that are produced in plants as a plant-pesticide. No evidence indicates that adverse effects due to aggregate exposure of nucleic acids with these substances through the dietary, non-food oral, dermal and inhalation routes occurs.

EPA considered exposure to nucleic acids produced in plants as a part of a plant-pesticide when it issued the proposal and it is not requesting additional comment on this topic. Comments are requested only on EPA's conclusion that there are no additional substances outside the food supply that are related, via a common mechanism of toxicity, to residues of nucleic acids produced in plants as part of a plant-pesticide for which EPA must consider exposure in aggregate with nucleic acids.

7. *Sensitivities of subgroups*. In 1994, EPA considered available information on the sensitivities of subgroups as it pertains to the nucleic acids produced in plants as part of a plant-pesticide in the proposal (59 FR 60542). The Agency's evaluation is summarized in Unit IV.A. of this supplemental notice.

8. *Naturally occurring estrogen or other endocrine effects*. FFDCA 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.

Based on available information concerning their structure and mode of action, EPA does not expect nucleic acids produced in plants as part of a plant-pesticide to cause estrogen or other endocrine effects. There is some information on estrogenic effects by exposure to pesticides but the data are limited and do not pertain to nucleic acids. If EPA becomes aware of a potential for estrogenic or endocrine effect from exposure to nucleic acids produced in plants as part of a plant-pesticide, EPA will reexamine this tolerance exemption 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 nucleic acids produced in plants as part of a plant-pesticide (59 FR 60542). As discussed in Unit IV.A. of this supplemental notice, EPA relied on the long history of safe human consumption of food containing nucleic acids produced in plants as part of a plant-pesticide 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 60542). 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 60542), EPA considered available information on the dietary consumption pattern of infants and children as it pertains to nucleic acids produced in plants as part of a plant-

pesticide 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. 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. All foods consumed by infants and children contain nucleic acids.

b. *Special susceptibility*. In the 1994 proposal (59 FR 60542), 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 nucleic acids produced in plants as part of a plant-pesticide. There is no scientific evidence that nucleic acids as a component of food would have a different effect on children than they would on the adult population. EPA summarizes its analysis of the effect of consumption in food of nucleic acids on human health 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 60542), EPA examined the available information on the cumulative effect of residues of nucleic acids produced in plants as part of a plant-pesticide 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 nucleic acids produced in plants as part of a plant-pesticide on 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 nucleic acids and other substances that have a common mechanism of toxicity.

Because EPA already considered the safety of food containing residues of nucleic acids produced in plants as part of a plant-pesticide and other constituents of food when it issued the proposal (59 FR 60542), the Agency is not requesting additional comment on that topic. Comments are requested only on EPA's conclusion that there are no substances outside of the food supply with a common mechanism of toxicity to the residues of nucleic acids produced in plants as part of a plant-pesticide.

d. *Margin of safety*. In determining whether the residues of nucleic acids produced in plants as part of a plant-pesticide 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 nucleic acids produced in plants as part of a plant-pesticide and other substances in food, 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 base of the human experience with actual food consumption 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 nucleic acids produced in plants as part of a plant-pesticide, 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 60542), EPA would exempt residues of nucleic acids produced in plants as part of a plant-pesticide. 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 residues of nucleic acids produced in plants as part of a plant-pesticide, indicates that adverse effects due to aggregate exposure through the dietary, non-food oral, dermal and inhalation routes occur.

The conclusion that residues of nucleic acids produced in plants as part of a plant-pesticide should be exempt from tolerance requirements under the FFDCA section 408 safety standard also lends support to EPA's proposed FIFRA exemptions (59 FR 60519) with respect to human dietary risks. These exemptions are: (1) Plant-pesticides that are derived from a plant that is sexually compatible with the recipient plant, (2) plant-pesticides that act primarily by affecting the plant, and (3) plant-pesticides that are coat proteins from plant viruses (59 FR at 60535). 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 the three categories of pesticidal substances subject to the proposed exemptions (59 FR 60535) and the nucleic acid component of a plant-pesticide (59 FR 60542) meet the FFDCA section 408 safety test, EPA concludes plant-pesticides in the three proposed categories of exemption 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 nucleic acids produced in plants as part of a plant-pesticide (59 FR 60542), EPA did not propose any numerical limitation on the amount of nucleic acids 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 and this supplemental notice and will consult with the Secretary of HHS prior to issuing the final rule. Because the 1994 proposal was an 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 nucleic acids in or on food is not required.

V. Comments

A. Confidential Business Information

Information submitted as a comment 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) EPA's conclusion that there are no substances outside of the food supply that may have a cumulative toxic effect with residues of nucleic acids produced in plants as part of a plant-pesticide.

(2) EPA's conclusion that there are no additional substances outside the food supply that are related, via a common mechanism of toxicity, to residues of nucleic acids produced in plants as part of a plant-pesticide for which EPA must consider exposure in aggregate with nucleic acids.

Commenters who possess information on nucleic acids causing estrogenic effects 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 containing nucleic acids produced in plants as part of a plant-pesticide 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 number ''OPP–300371A'' (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 number ''OPP–300371A.'' 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. 97–12786 Filed 5–15–97; 8:45 am]

BILLING CODE 6560–50–F

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[OPP–300367A; FRL–5716–6]

RIN 2070-AC02

Plant-Pesticides; Viral Coat Proteins; 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 the proposed exemption from the requirement of a tolerance under the Federal Food, Drug, and Cosmetic Act (FFDCA) for residues of coat proteins from plant viruses when these coat proteins are produced and used as plant-pesticides in plants or plant parts used as raw agricultural commodities. 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 viral coat proteins produced in plants as part of a plant-pesticide 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 viral coat proteins 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 that proposal.

DATES: Comments, identified by the docket number ''OPP–300367A,'' 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 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** documents. 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). Viral coat proteins produced in plants for viral coat protein mediated viral resistance are considered plant-pesticides because of their intended role in plant resistance to viral infection.

One of the five notices (59 FR 60545) proposed to exempt viral coat proteins produced in plants as part of a plant-pesticide, or segments of coat proteins, 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 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 viral coat proteins produced in plants as part of a plant-pesticide. For pesticidal substances in this category, many years of human experience with consumption of food containing plant viruses suggest that these pesticidal substances present negligible risk. Specifically, EPA proposed that ''residues of coat proteins from plant viruses, or segments of the coat proteins, produced in living plants as plant-pesticides are exempt from the requirement of a tolerance'' (59 FR at 60547).

This supplemental notice addresses the coat protein portion of the plant-pesticide 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 this supplemental notice may also affect EPA's final determination on a proposed exemption under FIFRA (59 FR at 60535) for plant-pesticides 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 viral coat proteins produced in plants as part of a plant-pesticide. 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