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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

January 31, 1997

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

PESTICIDE REGISTRATION (PR) NOTICE NO. 97 - 1

NOTICE TO MANUFACTURERS, FORMULATORS, PRODUCERS, AND REGISTRANTS OF PESTICIDE PRODUCTS

ATTENTION: Persons Responsible for the Registration and Reregistration of Pesticides

SUBJECT: Agency Actions under the Requirements of the Food Quality Protection Act

I. INTRODUCTION

The Food Quality Protection Act of 1996 (FQPA) requires the Environmental Protection Agency (EPA) to consider new factors when making pesticide regulatory decisions. Registrants, applicants, or petitioners for pesticide product registrations or reregistrations, or for tolerances or tolerance exemptions, whether pending or future, are advised to consider comprehensively the provisions contained in the Food Quality Protection Act (FQPA), specifically the factors relevant to aggregate exposure assessment, children's exposure, and other issues raised by the new statutory standard. This PR Notice explains to registrants how EPA will, on an interim basis, implement the new statutory provisions.

Although this PR Notice does not require registrants to submit any additional information, the Agency recognizes that because the Agency is required to consider additional information in order to make the necessary decisions, many registrants, applicants and petitioners may wish to provide the supplemental information to the Agency even without a requirement to do so. The Agency has already received a number of requests for information about the type of information that the Agency will need to consider under the new statutory provisions, as well as instructions for ensuring that the proper requests are updated with any supplemental information the registrant, applicant or petitioner wishes the Agency to consider. For those registrants, applicants or petitioners who wish to supplement their original submissions with additional information, the Appendices to this Notice describe what information the Agency would consider helpful, when and how material may be submitted to allow for the most efficient processing and review.[1]

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[1] The collection of information related to the registration, reregistration, and tolerance programs has been approved by the Office of Management and Budget (OMB) pursuant to the Paperwork Reduction Act under OMB Control Numbers 2070-0024; 2070-0032; 2070-0040; 2070-0060; 2070-0122; 2070-0107. These approvals cover the original submissions by the

II. APPLICABILITY

This Notice applies to most applicants with registration applications, non-crop-destruct experimental use permit applications, tolerance or tolerance exemption petitions, or reregistration eligibility decisions pending within the Agency. It also applies to most future applicants seeking new or amended pesticide registrations. This Notice includes all actions for synthetic chemicals, antimicrobials, biochemical and microbial pesticides. Those who may be affected are pesticide manufacturing companies, Interregional Research Project No. 4 (IR-4) petitioners, and other third party registrants. This Notice, however, does not apply to applicants seeking fast track "me-too" registrations or amendments not involving new uses.

Although the new standard in FQPA is clearly applicable to food use pesticides and chemicals related to such pesticides, EPA intends to apply a similar standard to actions involving non-food use pesticides that may pose significant non-dietary risks to infants and children.

III. EFFECTIVE DATE

This PR Notice is effective immediately.

IV. BACKGROUND

On August 3, 1996, the Food Quality Protection Act was signed into law. Effective upon signature, the new statute significantly amended the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug and Cosmetic Act (FFDCA). It was designed, among other things, to provide increased protection for infants and children from pesticide risks.

FQPA Title IV of the statute amends the Federal Food, Drug and Cosmetic Act. The most important aspect of this title is the establishment of a single, health-based standard for setting pesticide residue tolerances. This eliminates the longstanding problems posed by different standards for pesticides in raw and processed foods. The provision removes the requirement of food additive tolerances for processed foods and instead regulates them all under the same tolerance provision. A tolerance (or exemption from tolerance) for a pesticide residue on a raw agricultural commodity (RAC) also applies to residues in a processed food derived from the RAC that are not higher than the RAC tolerance. If the levels in the processed food are higher, a

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registrant, applicant or petitioner. In addition, EPA believes that the discussions within these existing Information Collection Requests also serve to cover any registrant's voluntary submission of information intended to supplement their original submissions.

separate tolerance must be set for that processed food. Residue levels in both the RAC and the processed food must be determined by EPA to be "safe."

The new safety standard, provided in section 408(b)(2)(A)(ii) of the statute, is a "reasonable certainty of no harm" standard for aggregate exposure using dietary residues and all other reliable exposure information. When setting new or reassessing existing tolerances or tolerance exemptions under the new standard, EPA must now focus explicitly on exposures and risks to children and infants. EPA must, 1) explicitly determine that the tolerance, or exemption from tolerance, is safe for children; 2) consider the need for an additional safety factor of up to ten-fold to account for uncertainty in the data base relative to children unless there is evidence that a different factor should be used; and 3) consider children's special sensitivities and often unique exposure patterns to pesticides.

In addition, when making a determination as to whether or not there is a reasonable certainty that a pesticide chemical will cause "no harm," EPA must now consider other non-occupational sources of pesticide exposure when performing risk assessments and setting tolerances. This includes dietary exposure from drinking water, non-occupational exposure, exposure from like pesticides that share a common mechanism of toxicity as well as other exposure scenarios. When setting new or reassessing existing tolerances and tolerance exemptions, EPA must also evaluate the potential for endocrine disruption. The new law directs the Agency to use its authority to require specific tests and information on estrogenic effects for all pesticide chemical residues.

Initial Communication to Registrants EPA began the task of implementing the requirements of the FQPA by explaining its goals and immediate plans in a letter sent August 21, 1996, to all current pesticide manufacturers, grower and other pesticide user groups, industry, environmental, consumer, and public interest groups. A second letter, containing more detailed information, was sent on September 6, to all holders of pesticide registrations. In its September 6 letter, the Agency stressed that work was continuing on many registration and reregistration activities and that interim decisions were being made. However, to ensure compliance with the new law's provisions to protect against pesticide uses which may pose unacceptable risks to children, additional time was needed to adequately review certain applications, especially food use applications. A letter has been sent to the States outlining the additional materials and information needed to make section 18 emergency exemption tolerance decisions.

Program Implementation - Status of Food Use Phase-in Process To deal with day-to-day decisions and procedural changes that must occur, EPA has identified key implementation processes on which to focus for all of the food and tolerance provisions of the Act. One area of immediate concern is phasing-in and applying the new requirements to currently pending registration, reregistration, and tolerance decisions. The Agency is inventorying all pending actions, and sorting them according to the applicable requirements of FQPA. The Agency estimates that there are more than a thousand actions pending at various stages of review. The

inventory of all the registration priority actions, biopesticide actions, and scheduled reregistration actions is almost complete. Criteria for ranking the inventory are being developed and, once actions are ranked, a process for handling each category will be devised and put into place.

V. INTERIM APPROACH TO RISK MANAGEMENT

The Food Quality Protection Act does not provide an explicit transition or phase-in period for many of the new requirements in the law. Some of the new requirements call for scientific analyses which have not been part of EPA's current risk assessment procedures. For example, traditionally EPA has assessed pesticide exposures separately by source and has not combined risks. Developing methodologies to address these issues requires a new way of approaching risk assessment and risk management.

While FQPA did not specify time frames for phasing in most of these provisions (with the exceptions of the 3-year time frame for developing a plan to assess endocrine effects, 1 year to develop an antimicrobial program, and a few others), the law contains sufficient flexibility to allow for a transition period while EPA develops new, long-term assessment practices. Congress, in discussions regarding the law, has confirmed this flexibility. EPA's goal even during this interim period is to fulfill the intent of the new law to increase the protectiveness of its regulatory process. While it is necessary to develop new assessment procedures and policies to implement the new requirements to the fullest, the Agency also needs to make timely decisions about the use of pesticide products. Delaying decisions does not achieve greater health protection and, in some instances, can cause harm. An interim decision logic allows decisions to be made now which are protective, more economic of resources, and which can be revisited as knowledge increases. EPA has designed an interim strategy to meet the new FQPA reasonable certainty of no harm standard in the absence of full data and fully developed exposure and risk assessment methodologies.

Interim Decision Logic for Aggregate Exposure The Agency's interim decision logic is a screening process for making regulatory decisions that are protective of public health and are workable within the current risk assessment practices with available data and methodologies. It also is designed to be flexible so that when actual data are submitted, earlier assumptions can be easily replaced with new information. Outcomes, at least initially, will be conservative and any approvals will most likely result in time limited or conditional decisions. As additional exposure data and improved methods and models are developed, decisions based on the interim logic will be revisited and modified as appropriate.

The new law says the Agency must now consider aggregate exposures from dietary and non-occupational sources when assessing the risks of a chemical and setting tolerances. In addition to dietary exposure, such sources as drinking water, residential and lawn care use need to be considered. For most pesticides, EPA has insufficient information on specific exposures through these routes. While new data are being generated and new exposure models developed, EPA will estimate the exposure components and risk, and allocate portions of that total aggregate

risk to drinking water, and residential and lawn use exposures (provided the pesticide is to be used indoors or on lawns). The remainder of the aggregate risk will be allocated to dietary exposure.

"The Risk Cup" EPA's interim decision logic is based on the concept that the total level of acceptable risk to a pesticide is represented by the pesticide's Reference Dose (RfD). This is the level of exposure to a specific pesticide that a person could receive every day over a seventy-year period without significant risk of a long-term or chronic non-cancer health effect. The analogy of a "risk cup" is being used to describe aggregate exposure estimates. The full cup represents the total RfD and each use of the pesticide contributes a specific amount of exposure that adds a finite amount of risk to the cup. As long as the cup is not full, meaning that the combined total of all estimated sources of exposure to the pesticide has not reached 100% of the RfD, EPA can consider registering additional uses and setting new tolerances. If it is shown that the risk cup is full, no new uses could be approved until the risk level is lowered. This can be done by the registrant providing new data which more accurately represent the risk or by implementing risk mitigation measures. While this explanation is focused on chronic non-cancer risk, the Agency will use a similar logic to assess acute risk and cancer risk.

The important issue for making interim decisions which take aggregate exposure into account is how much of the "risk cup" should be set aside or reserved for sources of possible exposure for which the Agency has limited or no actual data. Unless actual exposure data are available for these non-dietary pathways, the size of the "reserve" portion will be based on various characteristics of the pesticide, such as toxicity, mobility and persistence in soils, and use pattern. It has been decided that, in general, between 5% and 20% of the risk cup will be set aside for non-dietary exposures. The remainder of the risk cup will be left for dietary risk for which reliable data are available.

Interim Decision Logic for Common Mechanism of Toxicity Similar to the decision logic for aggregate exposure, the Agency has developed a conservative approach for assessing a common mechanism of toxicity for pesticides, ensuring that it is protective of public health, workable, and flexible for making timely regulatory decisions. If a pesticide shares a common toxicological endpoint and structural similarity with other substances, EPA will assume that a common mechanism of toxicity may exist. For such pesticides, any approvals will be time limited or conditional. As the Agency's understanding of common mechanism of toxicity increases, it will revisit such time limited or conditional decisions.

Making Interim Regulatory Decisions The decision logic for aggregate and cumulative risk, as described above, applies when EPA lacks data to estimate specific exposures from the various routes. If data were submitted which permitted a more precise estimate of exposure from a particular source, that information would be used to assign the appropriate portion of the risk cup for that source, rather than the more general default assumption. Further, if a registration or reregistration action did not pass the decision logic screen, additional data could be used to

reassess the risk or risk mitigation measures could be adopted which could lower the risk sufficiently to grant the action.

Using this interim decision logic, EPA is making regulatory decisions on pending actions, and registrants can now submit applications as instructed in the Appendices of this PR Notice. Over time, the decision logic will be revised and updated as new exposure data are generated. The interim decisions made will also be revisited, as necessary, based on new information and/or new methodologies.

VI. NEXT PR NOTICES

EPA places a very high priority on the development of new policies and procedures to implement the new law quickly and efficiently and to achieve its pre-enactment pace of regulatory activities. Even while activities resulting from this PR Notice are being put in place, work is continuing on many registration and reregistration activities, and interim decisions are being made. Biopesticide registration activities have continued although all pending tolerance actions have to be reannounced to meet the new FQPA requirements. For chemical pesticides, the Agency intends to issue a PR Notice requesting that registrants submit their next round of five priorities within several months. These priorities will include those required under the new law for minor use pesticides. The Agency also will be issuing a Notice similar to this one specifically directed to the minor use registrant community.

As the Agency works on a number of fronts to implement the new law fully and resume processing of all actions, it will provide registrants and applicants early and continuous information relating to their applications and petitions. The Agency also plans to issue a final document once it has gained significant experience in reviewing the applications and has put in place appropriate administrative procedures. The final document will include revised policy decisions and refinements of the items included in this PR Notice.

VII. FOR FURTHER INFORMATION

For further information, applicants may contact Stephen Johnson, Director, Registration Division at 703-305-5447; Lois Rossi, Director, Special Review and Reregistration Division at 703-308-8000; Janet Andersen, Director, Biopesticides and Pollution Prevention Division at 703-308-8712, or Frank Sanders, Director, Antimicrobials Division at 703-305-5440.

Date: JAN 31 1997

Daniel M. Barolo, Director
Office of Pesticide Programs

APPENDIX A

CONTENT OF SUPPLEMENTAL INFORMATION

As indicated at the beginning of the PR Notice, registrants, applicants and petitioners are not currently required to submit any additional information. Nevertheless, since the new statute requires the Agency to consider additional information in order to make the necessary decisions, EPA recognizes that many registrants, applicants and petitioners may wish to provide the supplemental information to the Agency even without a requirement to do so. For those registrants, applicants or petitioners who wish to supplement their original submissions with additional information, this Appendix describes what information the Agency would consider helpful additions for its review.[2]

All tolerances or tolerance exemptions and associated registration actions under FIFRA section 3 or reregistration actions under FIFRA section 4, whether pending or future, will need to comply with the new safety standard of section 408(b)(2) of the Federal Food, Drug and Cosmetic Act. In addition, because EPA intends to apply a similar standard to actions involving non-food use pesticides that may pose significant non-dietary risks to infants and children, all registration and reregistration actions also will need to comply with this standard with respect to the Agency's consideration of infants and children exposure to the pesticide.

In preparing a package to be submitted, those seeking a registration, reregistration, tolerance, or an exemption from the requirement of a tolerance for a food use pesticide, or a registration or reregistration of a non-food use pesticide that may result in significant exposure to children, may need to provide additional information and/or materials to address adequately the factors and specific questions contained here. Those who wish to submit additional information should keep in mind that the Agency will consider each factor listed below (and perhaps others as Agency policies are developed) in addition to any data and information already required. In addition, it is important to note that the information identified here may not be definitive in all cases. Additional information or more detailed information may be needed in individual cases. If a registrant, applicant, or petitioner can identify additional information that would assist the Agency in addressing the FQPA provisions, EPA welcomes such information. Although the submission of this information is not currently required by the regulations, if such information is

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[2] An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it either displays a currently valid OMB control number or is imposed on the person by statute (5 CFR 1320.6(a) & (e)). The collection of information relating to the registration, reregistration, and tolerance programs have are approved under OMB Control Numbers 2070-0024 (expires: 6/30/99); 2070-0032 (expires: 5/3/98); 2070-0040 (expires: 11/30/99); 2070-0060 (expires: 5/31/98); 2070-0122 (expires: 11/30/97); 2070-0107 (expires: 7/31/99). If you should have any comments on the collection activities, please send them to the Director, OPPE Regulatory Information Division, U.S. Environmental Protection Agency (Mailcode 2137), 401 M St., S.W., Washington, D.C. 20460. Include the OMB control number in any correspondence. Note that this address is ONLY for comments on the collection activity. Do not submit your information to this address.

not submitted, the Agency must rely on previously submitted data, if applicable, or on broad or default assumptions when considering the factors listed. As a result, favorable action on an application, petition, or reregistration decision may be significantly delayed or precluded altogether.

It would be helpful for any submitted documentation to contain a discussion of each of the following factors as it relates to the pesticide and proposed tolerance or tolerance exemption. If information on any factor is not known, that fact, along with an explanation, should be noted in the rationale. It is important to note that EPA does not expect the registrant, applicant, or petitioner at this time to perform any additional testing to derive the data necessary to develop its rationales. However, if it has in its possession data from preliminary reports of ongoing studies, articles from published literature, unpublished report information, previously unsubmitted studies, or supplemental data that are otherwise pertinent to the Agency's concerns, the party is encouraged to submit them. Likewise, if a registrant, applicant, or petitioner believes that a factor is not applicable to its product, a discussion as to why this view is held should also be included. The Agency will consider all relevant factors in determining an application's completeness and in setting priorities for review.

Based on the new safety standard, EPA will need the following additional information in order to make appropriate regulatory decisions: (For details on each factor, please refer to the explanations below in parts A and B.)

1. An informative summary of the petition or application, including a summary of the supporting data, information, accompanying rationales, and a statement providing permission to publish such summary, and

2. Information and discussion pertaining to a specific safety determination for infants and children including their special susceptibilities and exposure patterns to the particular pesticide.

A. Food Use Pesticides: Registration and Reregistration Actions, Experimental Use Permits, Tolerance (or Exemption) Petitions and Reassessments

In the format described in Appendix C of this PR Notice, address each of the following with respect to the pesticide and its use(s):

Special Sensitivities

a) Chronic Endpoints

For a chemical pesticide: Discuss and/or provide evidence as to whether or not the current Reference Dose (RfD) is sufficient to adequately protect infants and children. Discuss and/or provide evidence as to whether or not infants and children are more susceptible to the chemical. If you believe that an additional safety factor of 10X, to take into account potential pre- and post-natal toxicity to infants and children is not necessary, provide evidence to support the additional safety factor, if any, you believe to be more

appropriate. Please bear in mind that the Agency may accept a different margin of safety only if, based on reliable data, EPA concludes that the margin will be safe for infants and children.

For a biochemical pesticide:[3] Does the toxicity testing indicate that the establishment of an RfD is warranted? If so, then discuss whether or not the RfD is sufficient to adequately protect infants and children. Discuss and/or provide evidence as to whether or not infants and children are more susceptible to the biochemical pesticide.

For a microbial pesticide:[4] Discuss the potential for chronic dietary risks for infants and children. Discuss and/or provide evidence as to whether or not infants and children are more susceptible to the microbial pesticide than is the adult population.

b) Acute Endpoints

Discuss the potential for greater acute dietary risk for infants and children. If the chemical or biochemical pesticide demonstrates acute effects, then discuss the endpoint used to perform the assessment including relevance to infants and children and the details as to how the exposure assessment was conducted and whether the estimated risk is within the Agency's levels of concern.

c) Carcinogenic Endpoints

If the chemical or biochemical has been determined to be a carcinogen and has a cancer potency factor (Q_1*), discuss the aggregate excess lifetime cancer risk resulting from exposure to the chemical from residues in food and drinking water (ground and surface water) and from residential and other non-occupational source(s).

Aggregate Exposure

a) Water

For a chemical or biochemical pesticide: Discuss the potential for the transfer of residues (of both the parent pesticide and any degradates) to drinking water. The discussion should include, but not be limited to, information indicating whether the pesticide is persistent and/or mobile, relevant product chemistry, and any available modeling data.

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[3] A biochemical is a naturally-occurring compound, or substantially similar to a naturally-occurring compound, with a non-toxic mode of action to the target pest.

[4] Certain subpopulations are more susceptible to certain disease-causing microorganisms; however, these are not the types of microorganisms that are considered for registration or use as microbial pesticides. The Agency has not registered, and does not expect to register a microbial active ingredient that is known to be a common human pathogen. To address the potential risk from microbial pesticides, the Agency requires a battery of acute toxicity/pathogenicity studies in order to perform a risk assessment. If results of the acute exposure studies indicate a toxicity concern, then subchronic or chronic studies are required.