12/8/95

TO WHOM IT MAY CONCERN:

The attached draft PR Notice entitled "Toxicologically Significant Levels of Pesticide Active Ingredients" is being made available for public comment. The notice focuses on cross-contamination of active ingredients in pesticide products.

A Notice of Availability of this draft notice will be published shortly in the Federal Register which will invite public comment for a period of sixty days. If you have any comments, you may cite the Docket Number OPP-00424 and send them to:

By U.S. Mail:

Public Docket and Freedom of Information Section
Field Operations Division
Office of Pesticide Programs
U.S. Environmental Protection Agency (7506C)
Washington, D.C. 20460

Hand Delivered:

Public Docket and Freedom of Information Section
Field Operations Division
Office of Pesticide Programs
Room 1132, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202

If you have any questions about the implementation of this policy, you may contact Jim Jones at 703-308-8358. If you have questions regarding the analyses supporting this policy, contact Nancy Fitz at 703-305-7385.

Sincerely,

[Signature]

Stephen L. Johnson, Director
Registration Division
PESTICIDE REGULATION (PR) NOTICE 96-?

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

ATTENTION: Persons Responsible for Registration of Pesticide Products

SUBJECT: Toxicologically Significant Levels of Pesticide Active Ingredients

This notice sets out the Environmental Protection Agency's (EPA's) new risk-based approach for reporting "toxicologically significant" contaminants that are also pesticide active ingredients (AIs). The Notice establishes concentration levels of such contaminants that will generally be considered toxicologically significant in specified types of pesticide products. This draft Notice is subject to a 60 day comment period.

I. BACKGROUND

40 CFR 158.167 requires all impurities to be reported and approved/accepted by the Agency as part of the product's registration prior to the sale or distribution of the product containing the impurities in their products that are of toxicological significance. The introductory paragraph to § 158.167 states, in part, that "... If the applicant has reason to believe that an impurity that EPA would consider toxicologically significant may be present, the discussion must include an expanded discussion of the possible formation of the impurity and the amounts at which it might be present." Reporting is required for all impurities meeting this standard regardless of where the contamination occurred in the production and distribution processes.

EPA also requires applicants and registrants to propose certified limits (legally permissible amounts) for certain toxicologically significant impurities in pesticide products. If the product is a technical grade of active ingredient or is produced by an integrated system, 40 CFR 158.175(a)(3) requires that the applicant provide a proposed certified upper limit (the maximum legally permissible amount) for each impurity of toxicological significance associated with the active ingredient and found to be present in any sample of the product. In addition, EPA may, on a case-by-case basis, require certified
limits for other toxicologically significant impurities reported under § 158.167. Certified limits are set forth on the applicant's confidential statement of formula (CSF).

The preamble to the May 4, 1988 rule that promulgated 40 CFR 158.167 and 158.175 provided two sets of criteria for determining impurities having potential toxicological significance. The first was a list of specific substances known to be of toxicological significance. Among these categories, the Agency included "Any impurity that is also an active ingredient." (53 FR 15973) The Agency did not provide a numeric standard for determining the point at which these substances are considered "toxicologically significant." Rather, EPA has taken the position that any level of a chemical which is identified by the Agency as an active ingredient that is a contaminant in a product is of potential toxicological significance and must be reported to EPA or identified on the CSF.

If an AI is detected that is not on the CSF or that has not been reported as described above, then the registrant has violated section 12(a)(1)(C) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) because the registrant has distributed or sold a "registered pesticide the composition of which differs at the time of its distribution or sale from its composition as described in the statement required in connection with its registration under [FIFRA] section 3."

The policy announced in this notice refines the category of the existing definition of "toxicologically significant" regarding impurities that are active ingredients in other products by setting risk-based levels at which such substances will generally be considered "toxicologically significant." This policy does not address or alter any other portion of the existing definition.

Since 1992, several EPA Regions have conducted investigations to evaluate the extent of cross contamination of bulk pesticides. An important part of applying the 40 CFR Part 158 standards to bulk pesticides at repackaging/refilling establishments (often retail dealers) is EPA's interpretation of the Bulk Pesticides Enforcement Policy (Bulk Policy) dated July 11, 1977 and amended on March 4, 1991. Nothing in this policy changes the conditions outlined in the Bulk Policy for the two parties involved (registrant and repackager.) In particular, EPA's position that both parties are accountable for the integrity of the product as set out in the Bulk Policy remains the same. For example, even when the contamination occurs at the bulk repackaging facility both parties remain responsible for the integrity of the product.

As a result of many questions and comments from EPA Regions, States and the regulated industry, the Office of Pesticide
Programs has re-evaluated EPA's current position on cross contamination as described above. As a result of this work, EPA is revising its interpretation of "toxicologically significant" levels of AIs to be the risk-based levels set out in section IV. However, this policy only addresses impurities that are also AIs, i.e., a subset of the universe of impurities. Specifically, for the purposes of this policy, a contaminant is defined as an AI that is not on the product's confidential statement of formula or listed in the discussion of impurities. EPA's position on other impurities has not changed.

II. OBJECTIVES

EPA determined that a policy on cross contamination should:

Ensure that allowable cross contamination does not pose unreasonable adverse effects;
Recognize that cross contamination is a reality, and that not all cross contamination is problematical;
Set a clear standard that can be readily applied by EPA/States and the regulated industry alike;
Be easy to administer in that it minimizes the paperwork burden for EPA and registrants;
Maintain accountability for the product from the registrant to the end user;
Minimize the possibility that cross contamination will pose a significant problem, but
Allow for easy and equitable enforcement when toxicologically significant cross contamination is found, and
Not preclude marketplace/private solutions to correct problems that do arise.

III. APPROACH

EPA decided that a risk-based approach would be most likely to meet these objectives and to define an acceptable policy. One risk-based option would be to consider each case of cross contamination individually after it had been detected, to evaluate the potential risks (e.g., to humans, birds, aquatic organisms, plants, etc.) and to determine if any of EPA's levels of concern were exceeded. However, EPA rejected this option because it would be too resource-intensive and would address this issue after harm occurred as opposed to preventing the potential for harm.

Instead, EPA considered the risks for several endpoints, including human health, violative residues, contamination of ground water and ecological effects to determine which endpoints would be most sensitive to cross contamination and what levels of cross contamination could be tolerated and remain generally protective of human health and the environment. For each
endpoint, an analysis was done to evaluate a reasonable worst case scenario or a range of potential scenarios to see if an overall, generally protective contaminant concentration could be determined. EPA grouped contaminants and pesticides into different categories (see the table in section IV), to yield a scheme of toxicologically significant concentrations.

The following is a brief description of the end points that were considered. In most cases, it appears that phytotoxicity to the target plants is the most sensitive endpoint and, therefore, the limiting factor in determining toxicological significance.

Human health effects. Because cross contamination is most likely an intermittent event, short-term exposure is most likely. Therefore, EPA believes that the potential for chronic human health effects from cross contamination is negligible. EPA focused on the potential risks to individuals who would be handling contaminated products. The analyses of these human health risks show that acute risks to humans at the cross contamination levels allowed by this interpretation are also negligible. EPA also considered contamination in pesticides applied to the human body.

Violative residues. EPA evaluated the potential for cross contamination to result in violative residues in food or feed. Theoretically, it is possible that a contaminant could be detected in food or feed and for there to be no tolerance for the contaminant pesticide. EPA's analysis indicates that this is a highly unlikely scenario. In addition, because cross contamination occurs intermittently and would be at low levels, EPA believes that dietary risk from the potential residues allowed by this interpretation would be negligible.

Ground water. The possibility of the contamination of ground water was raised as a potential concern in locations with sandy soils and shallow aquifers. The Florida Department of Agriculture and Consumer Services (DACS) conducted a preliminary ground water modeling exercise using a number of conservative assumptions regarding leachability, pesticide half-life, and product application rate. The Florida DACS concluded that, while contamination of ground water was possible, it was of minimal concern because pesticide AIs at the levels allowed by this notice are unlikely to move to ground water in concentrations that would pose significant risk to human health.

Ecological effects/phytotoxicity. Based on a preliminary review of potential ecological effects from cross contamination (e.g., risks to birds, aquatic organisms and plants), EPA believes that plant toxicity, or phytotoxicity, is the most sensitive endpoint given the relatively low concentrations of pesticides being considered and poses the greatest potential for harm. The phytotoxicity analyses described below focused on the
direct application of the contaminated product to terrestrial plants because this scenario represents a higher level of exposure than other exposure pathways, such as runoff and drift.

IV. TOXICOLOGICALLY SIGNIFICANT LEVELS OF CONTAMINATION

The following table defines the levels of contaminants that EPA considers to be toxicologically significant. Specifically, the presence of a contaminant at a concentration greater than the concentration specified in the table would generally be considered toxicologically significant. Each contaminant should be considered individually. The basis for each category is described in section V below.

**Toxicologically Significant Levels of Contaminants**

<table>
<thead>
<tr>
<th>Category</th>
<th>Scenario</th>
<th>Toxicologically Significant Level (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Insecticide, rodenticide or fungicide in any insecticide, fungicide or herbicide</td>
<td>1000</td>
</tr>
<tr>
<td>2</td>
<td>Herbicide in any pesticide where the contaminant is accepted for use on all crops for which the product is labeled.</td>
<td>1000</td>
</tr>
<tr>
<td>3</td>
<td>Any pesticide other than a low application rate herbicide in an antimicrobial pesticide</td>
<td>1000</td>
</tr>
<tr>
<td>4</td>
<td>Standard herbicide in any herbicide</td>
<td>250</td>
</tr>
<tr>
<td>5</td>
<td>Standard herbicide in any insecticide or fungicide</td>
<td>100</td>
</tr>
<tr>
<td>6</td>
<td>Low application rate herbicide in a low application rate herbicide</td>
<td>Level of quantification or 100 ppm, whichever is higher</td>
</tr>
<tr>
<td>7</td>
<td>Low application rate herbicide in a standard herbicide</td>
<td>Level of quantification or 20 ppm, whichever is higher</td>
</tr>
<tr>
<td>8</td>
<td>Any pesticide in a pesticide applied to the human body</td>
<td>10</td>
</tr>
<tr>
<td>9</td>
<td>Low application rate herbicide in a pesticide other than a herbicide</td>
<td>Level of quantification or 1 ppm, whichever is higher</td>
</tr>
</tbody>
</table>

Notes:
1. This column presents the toxicologically significant level, i.e., the concentration above which EPA would consider the contaminant to be toxicologically significant.
2. The FIFRA definition of insecticides includes miticides.
3. For the purposes of this policy, a contaminant is defined as an AI that is not on the product’s confidential statement of formula (CSF) or listed in the discussion of impurities.
4. For the purposes of this proposal, a standard herbicide is defined as a herbicide with a maximum labeled application rate of AI on labeled crops >0.5 pounds AI/acre.
5. For the purposes of this proposal, a low application rate herbicide is defined as a herbicide with a maximum labeled application rate of AI on labeled crops ≤0.5 pounds AI/acre.
6. For purposes of this notice, the level of quantification is the level of quantification achievable by EPA at the time the analysis is performed.

In establishing levels of toxicological significance, EPA realizes there is a trade-off among competing factors. A lower standard would be more protective, but would lead to higher compliance costs for the industry, higher implementation costs for EPA and the industry (e.g., the submission of expanded discussions of impurities in many cases instead of just a few), and the potential for fewer products available for users. When evaluating the results of the analyses discussed in section V, EPA attempted to find a reasonable balance between these competing factors. If future experience indicates that these values are not sufficiently protective, the Agency may find it appropriate to modify these levels of toxicological significance.

EPA believes the values in the table are generally protective in most contaminant/product combinations. Because it is impossible to consider every potential contaminant/product permutation, adverse effects could occur when contamination is present at or below the concentrations in the table.

The Agency recognizes that the proposed standards will not prevent all possible adverse effects from occurring; this is not a zero risk standard. For example, EPA is aware of a situation where a standard herbicide (norflurazon) contaminated an insecticide (insecticidal soap for use on home and garden plants) at levels below 100 ppm (as set out in Category 5) and plant damage occurred. The Agency will continue to deal with such situations using other regulatory tools including section 6(a)(2) of FIFRA.

Accordingly, this policy does not excuse applicants or registrants from the requirement to submit to EPA factual information regarding unreasonable adverse effects of a pesticide under section 6(a)(2) of FIFRA and EPA regulations at 40 CFR 152.50(f)(3). If an applicant or registrant possesses factual information not previously reported to EPA indicating that a contaminant in a product may pose risk to human health or the environment in concentrations lower than those specified in the above table, that information must be submitted to EPA. Failure to submit such information on a timely basis is a violation of sections 12(a)(2)(B)(ii) and 12(a)(2)(N) of FIFRA. In addition,
the distribution or sale of any product containing an unreported contaminant for which the registrant has failed to submit additional factual information regarding unreasonable adverse effects is a violation of section 12(a)(1)(C) (composition differs) of FIFRA.

V. DISCUSSION

This section summarizes the analyses that support the toxicologically significant levels in the above table. For more details, refer to the full analyses (see section VIII). EPA believes these analyses represent reasonable worst case or representative scenarios. Because it was impossible to consider every potential contaminant/product permutation, however, the analyses are necessarily limited in scope.

Category 1. Because phytotoxicity is generally not a major concern with insecticides or fungicides, the limiting endpoint for this category is potential adverse effects to human health. EPA conducted a risk assessment assuming a fungicide was contaminated with 1000 ppm of an insecticide, fungicide and herbicide (each individually). Exposure to mixer/loaders and applicators during airblast and aerial treatment was analyzed because these application methods would likely result in the greatest potential worker exposure. Based on this limited analysis, EPA concludes that adverse effects to human health occurring from cross contamination at 1000 ppm are very unlikely to occur. It is, however, theoretically possible that certain exposure scenarios may present risks which exceed EPA's levels of concern (LOC's), e.g., when highly acutely toxic pesticides contaminate products that require the use of limited personal protective equipment. However, EPA believes that contamination at or below 1000 ppm generally is not of toxicological concern from a human health perspective. (References 1 and 2)

With the exception of pesticide products that are intentionally applied to the human body (see category 8), other user scenarios involving cross contamination were considered and were found to pose negligible risk to human health. (Reference 3)

EPA also evaluated the potential for illegal residues as a result of cross contamination. The conditions that are most likely to result in possible violative residues are when application rates are high, pre-harvest intervals are short and the harvested crop can be expected to have high tolerance values. However, actual residues on commodities rarely approach the legal tolerances. An examination of Food and Drug Administration surveillance data for the example fungicide on several commodities shows that actual residues are usually far below the tolerances (250 - 5700 times less in this case). Therefore, EPA believes that it is highly unlikely that illegal residues from cross contamination at or below 1000 ppm would be found. It is
important to note, however, that food or feed containing residues from cross contaminants may be adulterated pursuant to section 402 of the Federal Food, Drug, and Cosmetics Act (FFDCA) unless there is a tolerance covering the residue. (References 1 and 2)

Category 2. The limit in category 2 is based on the assumption that it is safe to apply 1000 ppm (0.1% by weight) of a herbicide to a crop or site for which the herbicide is labeled for use. The herbicide that is the contaminant in this case will be present at a much higher concentration when it is an intended AI in a pesticide product used on the same crop or site.

Category 3. Similar to the analyses supporting category 1, EPA considered an apparently worst case scenario -- contamination of an antimicrobial pesticide with an insecticide (azinphos-methyl) at 1000 ppm. The estimated maximum exposure was based on a Chemical Manufacturers Association exposure assessment study of a wide variety of use sites and application methods. The exposure to the insecticide did not exceed EPA's LOC. Based on this limited analysis, EPA concludes again that adverse effects to human health occurring from cross contamination at 1000 ppm are very unlikely.

Categories 4-9. The remaining five categories (with the exception of category 8) involve herbicides as the contaminants and the levels of toxicological significance are based on phytotoxicity analyses. The categories are distinguished by whether the contaminant is a standard or a low dose herbicide and by the type of product that is contaminated. While the distinction between standard and low dose herbicides is based on the AI application rate, the two categories represent different levels of plant toxicity. Low dose herbicides generally are phytotoxic at lower levels than standard herbicides. Therefore, these AIs can be applied at lower rates than standard herbicides. A corollary is that, when a low dose herbicide is the contaminant, a relatively low concentration is toxicologically significant. The category of low dose herbicides generally includes chemicals classified as sulfonylureas, imidazolinones and triazolopyrimidines.

The type of product that is contaminated also affects the level of contaminant that would be toxicologically significant. In most cases, insecticides and fungicides are applied more often and at higher rates than standard herbicides, which are applied at higher rates than low dose herbicides. For example, a given herbicide contaminant would be present in similar quantities on a particular crop if it was present in a fungicide at a low concentration and in a standard herbicide at a higher concentration.

Category 4. Category 4 is based on an analysis of 25