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

SEP 29 1981

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

PR NOTICE 81-3
NOTICE TO MANUFACTURERS, FORMULATORS, DISTRIBUTORS, AND REGISTRANTS OF PESTICIDES

ATTENTION: Persons Responsible for Federal Registration of Pesticides

SUBJECT: Label Improvement Program: Change in Test Methods for and Categorization of Eye Irritation

This Notice announces EPA's adoption of new testing methods for, and categorization of, eye irritation. Registrants will not be required to adhere to this policy until reregistration. Therefore, until that time, no action on the part of registrants to relabel current products will be required. ~~Applicants, although not required,~~ are encouraged to label ~~their products in accordance with the new criteria~~ in order to ~~avoid~~ relabeling for this purpose at the time of reregistration.

I. Background

In 1975, EPA established in 40 CFR 162.10(h) toxicity categories which are based on the results of acute toxicity tests. The criteria for eye irritation categorization in the 1975 regulation are based on a seven-day observation period.

In 1977, the National Academy of Science (NAS) published a revised version of its 1964 document entitled "Principles and Procedures for Evaluating Toxicity of Household Substances" commonly known as the NAS Publication 1138. NAS concluded, on the basis of studies submitted, that for adequate evaluation of the effects produced when chemicals are introduced into the eyes of animals, an observation period of three weeks was necessary. In addition to a classification scheme for eye irritation severity based on a three-week observation period, the NAS recommended that the reversibility of the effects within that period be considered in classifying substances.

II. Change in Methodology and Criteria for Toxicity Categories for Eye Irritation

The Agency is adopting the NAS recommendations and revising its 1975 eye irritation criteria accordingly. Studies will be evaluated, and categories assigned, based on a twenty-one day observation period including reversibility of effects over that period. Toxicity categories for eye irritation are now defined as follows:

I	II	III	IV
Corrosive (irreversible destruction of ocular tissue) or corneal involvement or irritation persisting for more than 21 days	Corneal involvement or irritation clearing in 8-21 days	Corneal involvement or irritation clearing in 7 days or less	Minimal effects clearing in less than 24 hours

III. Change in Precautionary Labeling for Eye Irritation

The Agency has also revised its precautionary labeling statements for eye irritation to reflect NAS criteria. These statements are in the Appendix.

IV. Optional Retesting and Amended Registrations

1. Registrants are not required at this time to retest their products or submit applications for amended registration. Only when a registration standard is issued for the active ingredient in a product will registrants be required to comply with this policy.

2. In certain cases registrants may have previously submitted studies that justify reclassification of products to a lower toxicity category (e.g., I to II, or II to III) due to the reversibility of effects. In such cases registrants are encouraged to refer the Agency to these existing tests and amend their labels accordingly.

3. Any registrant may conduct a new eye irritation study with a twenty-one day observation period and request that his product be recategorized according to the new criteria. This course might be chosen if the registrant believes that the twenty-one day observation period will permit assignment to a lesser toxicity category (e.g., I to II).

4. If a registrant wishes to have the Agency consider new data on eye irritation, and concomitant label changes, an application for amended registration must be submitted to the appropriate Product Manager in the Registration Division. This may be done at any time. An amended registration for this purpose must contain:

   a. EPA form 8570-11 (Application for Amended Registration);

   b. Two copies of new eye irritation studies; and

   c. Two copies of draft labeling incorporating revised precautionary statements. The Appendix to this notice provides precautionary statements that are to be used for this purpose.

V. Implementation

A. Testing

Applicants/registrants may proceed at this time with eye irritation studies based on the new testing criteria. The observation period must be such as to allow a conclusive demonstration as to whether eye effects are reversible within or persistent beyond 21 days.

B. Categorization of Products

1. The Agency will begin immediately to evaluate products according to the new criteria.

2. However, in many instances, new data will not be available immediately. Therefore, in the interim, products will be categorized on the basis of data presently available. That is, if

all effects are reversible within 7 days, the products will be assigned to Toxicity Category III. If any effects persist beyond 7 days, the product will be assigned to Toxicity Category II or I. No product, however, will be assigned to Toxicity Category II based on a study terminated on the 7th day, since the Agency is unable to distinguish Category I from II on the basis of seven-day studies.

VI. Further Information

For further information on the revised testing methodology, persons may contact Dr. Reto Engler, Registration Division (TS-767C), EPA, 401 M Street, S.W., Washington, DC 20460, phone number 202-557-7161.

For information on applications for amended registration, registrants may contact the appropriate Product Manager in the Registration Division.

Douglas D. Campt
Director
Registration Division (TS-767C)

APPENDIX

LABEL STATEMENTS REGARDING EYE IRRITATION HAZARDS DUE TO PESTICIDES

TOXICITY CATEGORY	SIGNAL WORD	SKULL AND CROSSBONES & "POISON" REQUIRED	PRECAUTIONARY STATEMENTS	PRACTICAL TREATMENT
I Corrosive; (irreversible destruction of ocular tissue) or corneal involvement or irritation persisting for more than 21 days.	DANGER	No	Corrosive.* Causes irreversible eye damage. Harmful if swallowed. Do not get in eyes or on clothing. Wear (goggles, face shield, or safety glasses).** Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash before reuse.	If in eyes: Flush with plenty of water. Get medical attention. If swallowed: drink promptly a large quantity of milk, egg whites, gelatin solution, or, if these are not available, drink large quantities of water. Avoid alcohol. NOTE TO PHYSICIAN: Probable mucosal damage may contraindicate the use of gastric lavage.
II Corneal involvement or irritation clearing in 21 days or less.	WARNING	No	Causes substantial but temporary eye injury. Do not get in eyes or on clothing. Wear (goggles, face shield, or safety glasses).** Harmful if swallowed. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash before reuse.	Same as above except omit NOTE TO PHYSICIAN statement.
III Corneal involvement or irritation clearing in 7 days or less.	CAUTION	No	Causes (moderate) eye injury (irritation). Avoid contact with eyes or clothing. Wash thoroughly with soap and water after handling.	If in eyes: Flush with plenty of water. Get medical attention if irritation persists.
IV Minimal effects clearing in less than 24 hours.	CAUTION	No	None required.	None required.

*The term "corrosive" may be omitted if the product is not actually corrosive.

**Choose appropriate form of eye protection. Recommendation for goggles or face shield is more appropriate for industrial, commercial, or non-domestic uses. Safety glasses may be recommended for domestic or residential uses.

Certain older methods of analysis (such as the total chlorine and acid methods) determine the amount of label-declared active ingredients as including any related compounds that are not separately identified in the ingredients statement. Newer, more specific AOAC methods (such as high pressure liquid chromatography) are more discriminating and are able to distinguish between the intended active component and the related compounds that were previously indistinguishable. Use of more specific methods of analysis for enforcement purposes without modifying label ingredients statements would indicate that the active ingredient content is less than the current label declaration. The product therefore would appear deficient and might be subject to the misbranding provisions of FIFRA. Several states in their pesticide enforcement programs have already set deadlines for product/labeling compliance using newly approved AOAC methodology.

The purpose of this notice is to delineate a uniform policy and procedure for resolution of these problems.

II. APPROACH

The Agency is clearly in favor of greater accuracy in definition and declaration of pesticide ingredients. When AOAC methods are changed the Agency must consider either requiring the registrant to change pesticide labeling and confidential statements of formula or allowing changes in the chemical composition of the pesticide itself. The Agency considers unacceptable the "spiking" or overformulation of the formulated product with additional active ingredient solely to compensate for apparent deficiencies resulting from new analytical techniques. Moreover, such an approach could significantly increase Agency review time by triggering evaluations for potential increased hazard to the environment unless label dosage rates were proportionally decreased.

For some chemicals, new methods do not exist or new methods of analysis will continue to evolve. In order to deal with this changing situation, a flexible regulatory approach is needed. Such an approach must accommodate this evolutionary process while supporting enforcement activities and resulting in minimum impact on the environment, on the regulatory review process, on pesticide use patterns and on registrants.

Samples collected by Federal inspectors pursuant to FIFRA or by State inspectors under the Pesticide Enforcement Grant Program are analyzed by official methods when such methods exist. As new methods are developed and evaluated, these may become official AOAC methods replacing the old methods. Superseded methods are no longer considered official. If old and new methods give the same results, both methods maintain official status and either may be used in the analysis of potentially violative samples. In other situations where the official AOAC analytical method represents improved definition of ingredients

and creates discrepancies between analytical results and existing label ingredients statements, the Agency will issue notifications to registrants to accommodate the new official AOAC method.

The Agency's approach entails an appropriately timed revision of label ingredients statements and revision of confidential statements of formula to reflect the minimum percentage of each active component as determined by newly accepted AOAC methods of chemical analysis and, as appropriate, the inclusion of related compounds in the inert ingredients.

III. POLICY

A. For purposes of this notice the term "label ingredients statement" includes not only the percentages of active and inert ingredient(s), but also, if applicable, associated acid or metallic equivalents and quantity of active ingredient(s) per volume of liquid formulation.

B. Related compounds no longer indistinguishable from the intended active ingredient(s) due to newer, more discriminating methods of analysis must be accounted for within the pesticide label ingredients statement. The active or inert status of each ingredient including these related compounds is determined according to 40 CFR 162.6(b)(2)(i)(C)(2). Such determination is the responsibility of the registrant. If one or more related compounds is isolated and found to be active, it must be specifically identified and quantified by percentage under the active ingredient heading of the label ingredients statement. Those related compounds whose active/inert status is not determined by the registrant must be included (without designation as related compounds or by name) within the total percentage of inerts in the label ingredients statement.

C. Unless declared as active ingredients, related compounds will not be included in expressing percent acid or metallic equivalents, nor in the declaration of pounds active ingredient or acid equivalent per gallon in the label ingredients statement.

D. On the other hand, references to weight of active ingredient per volume of liquid and references to percent of active ingredient found in the product name, such as 4L, 3AS, 80W, or 10G, need not be changed as a result of altering the method of analysis.

E. Confidential statements of formula must indicate the appropriate AOAC method number for each active component affected by this notice. Since the method numbers are periodically revised by the AOAC, the AOAC manual edition must be specified. Methods of analysis will not be considered confidential.

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SEP 30 1981

PR Notice 81-4

NOTICE TO PRODUCERS, REGISTRANTS AND FORMULATORS

Attention: Persons Responsible for Federal Registration of Pesticides

Subject: Label Improvement Program: Label Revisions to Accommodate New AOAC Methods of Chemical Analysis

This Notice describes procedures that will be used to ensure that pesticides label ingredients statements reflect percentages of ingredients determined by the most specific chemical analytical techniques approved by the Association of Official Analytical Chemists (AOAC). These procedures potentially affect all registrants since AOAC methods for a wide range of chemicals are continually being reviewed and modified. This Notice is a statement of policy. NO SPECIFIC ACTION IS REQUIRED UNTIL REGISTRANTS ARE NOTIFIED INDIVIDUALLY.

I. BACKGROUND

All pesticide products are required to bear a label ingredients statement, including the identification and percentage of each active ingredient and the total percentage of inert ingredients. Methods for pesticide chemical analysis are refined and standardized by the AOAC on a continuing basis. Consequently, pesticide labels that are revised infrequently do not always reflect analyses by the most definitive AOAC methodology. This situation can lead to difficulties in pesticide enforcement, in label consistency, and in coordination between state and Federal programs.

IV. PROCEDURES

Procedures established for the Label Improvement Program (45 FR 37884, June 5, 1980) will be followed, with the following modifications:

A. A Confidential Statement of Formula (EPA Form 8570-4) will be required for each product, and will be reviewed for compliance with Section III.E. of this Notice. This Notice does not negate any previous requirements relative to Confidential Statements of Formula.

B. Applications will be considered non-compensable, i.e., not subject to the provisions of FIFRA 3(c)(1)(D), provided no changes are made other than those required by this Notice. Therefore, no Offer to Pay or Certification Statements will be required to be submitted.

C. Because of the nature of the revisions resulting from analytical method changes, and in order to ensure that formulators and repackagers can reference Agency-accepted Confidential Statements of Formula, basic pesticide producers will be required to comply before formulators and repackagers of end-use products. Phased notification will allow producers to advise their formulators of Agency-accepted labeling and should provide a more orderly and efficient processing of information within the Agency.

REGISTRANTS OF AFFECTED PRODUCTS WILL BE NOTIFIED WHEN TO SUBMIT APPLICATIONS. THIS NOTICE DOES NOT REQUIRE ACTION BY REGISTRANTS UNTIL NOTIFIED. However, we emcourage early submission of amended applications whenever registrants become aware of new AOAC official methods. A more rapid review can be done if applications are submitted on a phased basis by registrants rather than awaiting a notice requiring specific compliance times.

Questions concerning the policies or procedures in this Notice may be directed to Dr. Thomas Ellwanger, by telephone (703) 557-1650.

Douglas D. Campt
Director
Registration Division (TS-767C)

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

JAN 12 1982

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

PR NOTICE 82-1

NOTICE TO MANUFACTURERS, FORMULATORS, DISTRIBUTORS,
AND REGISTRANTS OF PESTICIDES

Attention: Persons Responsible for Federal Registration of Pesticides

Subject: Revised Policy on Label Claims for Tank Mixing

This notice announces that EPA has revised its policy for approving tank mix claims on pesticide labeling. This policy supersedes that contained in PR Notice 69-8, dated April 21, 1969.

I. Background

In the past, the Agency has required that applications for new registration or for amended registration involving claims for tank mixing the pesticide product with another pesticide product be supported by compatibility data and, if the mixture is to be used on a food or feed crop, by residue data demonstrating that the mixture would not result in residues higher than the tolerance established for each active ingredient. However, in cases where the pesticide labels are silent on the matter of tank mixing, applicators have been permitted to use tank mixes at their own risk if the sites or crops on which the mix is to be used are registered sites and crops for all the pesticides contained in the mix and if all pertinent limitations, use directions, and precautions are followed.

Since years of reviewing compatibility and residue data for tank mixes and records of actual field experience have shown that as a practical matter potentiation is not likely to occur and that the resulting residues are within established tolerances, the Agency has revised its policy with respect to the requirements that must be met before label claims for tank mixes can be approved. This revised policy will significantly reduce the data generation burden on registrants as well as the review burden on the Agency and thus will allow more expeditious approval of registrations involving tank mix claims.

II. Policy

EPA will usually approve tank mix label claims without supporting compatibility and residue data if the following conditions are met:

(1) The site(s) or crop(s) for which tank mix claims are made are registered crops or sites for all pesticides recommended in the mix.

(2) The chemical characteristics of all products to be used in the mix are such that no incompatibility or potentiation is likely to occur. (The Agency reserves the right to request appropriate data if it determines that a problem could arise.)

(3) The pesticide product to be mixed with the product which is the subject of the application does not contain a label prohibition against such mixing.

and (4) The label contains the statements: "This product can be mixed with _____ (chemical name, including percentage of active ingredient and type of formulation, or specific product name, or both) for use on _____ (crops/sites) in accordance with the more (most) restrictive of label limitations and precautions. No label dosage rates should be exceeded. This product cannot be mixed with any product containing a label prohibition against such mixing." Variations of these statements may be approved by the Agency. Where a specific product name is recommended for the tank mix, the label statements shall be more explicit, including such information as specific dilution and dosage rates.

It should be noted that the addition of tank mix claims to labels still requires Agency review and approval prior to distribution. It should also be noted that although EPA will not as a rule require submission of efficacy, compatibility, or residue data to support tank mix claims, applicants and registrants should assure themselves that such tank mixes will not result in compatibility problems or residues in excess of tolerances.

III. Relationship to Recommendations Made Under FIFRA Section 2(ee)

On October 22, 1981, the Agency published in the Federal Register a policy stating that recommendations or advertisements for FIFRA section 2(ee) uses may be made even though the pesticide product label is silent with respect to such uses (46 FR 51745). Of relevance to this notice is section 2(ee)(4), which states that it is not a misuse to mix a pesticide or pesticides with a fertilizer when such mixture is not prohibited by the labeling.

The Agency wishes to clarify that this particular provision of the Act, as interpreted by the Federal Register notice, allows any person to make tank mix recommendations for use on crops or sites listed on the labels of both pesticide products regardless of whether or not the labels contain tank mix claims; however, in no case may tank mix recommendations be made for products containing label prohibitions against such claims. With respect to recommendations involving the dilution rate of the pesticides in the tank mix, the total amount of diluent used must not be less than the amount required for the product requiring the higher rate of dilution. Recommendations for applying tank mixes for agricultural or forestry purposes at a dilution rate less than the higher of the label rates may be made only in accordance with the Advisory Opinion published in the Federal Register on March 3, 1981 (46 FR 14965).

IV. Effective Date

This policy is effective immediately.

V. Further Information

Further information on this policy can be obtained from Tom Adamczyk (703-557-1650) or from the appropriate Product Manager.

Douglas D. Campt
Director
Registration Division (TS-767-C)