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

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

Fax On Demand
Item Number

January, 8 2001

PESTICIDE REGISTRATION (PR) NOTICE 2001-2

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

ATTENTION: Persons Responsible for the Registration and Reregistration of Pesticides

SUBJECT: Acute Toxicity Data Requirements For Granular Pesticide Products, Including Those With Granular Fertilizers in the Product.

This PR Notice announces guidance intended to streamline the acute toxicity review and classification process for certain granular pesticide products, including those products that contain granular fertilizers. Based on OPP's extensive experience with granular pesticide products, the Agency believes that an effective precautionary labeling policy can be implemented without testing of each individual product. Please refer to Section IV on how OPP will implement this guidance. This guidance is supported by a large toxicology data base and involves the application of sound scientific principles. This guidance should achieve the following objectives: (1) significantly reduce the number of animals subject to testing; (2) reduce the use of Agency resources while maintaining protection of the public health and environment; and (3) decrease the time required to register qualifying granular pesticide products. This notice is effective immediately, but comments will be accepted for 30 days, after which the Agency may revise the notice.

I. Background

FIFRA and Agency regulations require that each pesticide product bear on the label danger, warning or caution statements. The signal word and precautionary statements are based on the acute toxicity category of the pesticide, which is designed to protect the public health. This labeling informs pesticide users/workers of the acute health hazards from exposure to the pesticides and what

precautions should be taken to mitigate adverse effects. To determine the appropriate human hazard signal word and label instructions the Agency evaluates six acute toxicological studies: acute oral toxicity (870.1100), acute dermal toxicity (870.1200), acute inhalation toxicity (870.1300), eye irritation (870.2400), dermal irritation (870.2500) and dermal sensitization (870.2600). The Series 870 numbers are the new guideline numbers which previously appeared in 40 CFR 158.340 as guidelines § 81-1 through § 81-6.

Pesticide products are generally composed of the active ingredient(s) and inert ingredient(s). This notice refers to those granular pesticide products that are composed of a registered source product at less than 10% active ingredient, one or more clearly recognized innocuous (List 4) inert carrier(s) and/or a fertilizer component(s) at greater than 90% and a sticker/binder (5% of the formulation). Innocuous inerts (List 4) are carriers that are considered to be chemically inactive based on available information and experience. Inerts in this category include corncobs, clay, limestone, sand or food, etc.

This policy only applies to granular pesticide products and granular fertilizer pesticide products. The Agency will not extrapolate for other products, because; 1) the LD_{50} is imprecise (dilution does not always equal reduced toxicity); 2) a complete dose response curve, required at a minimum, is rarely available; and 3) the Agency does not have a database that indicates that dilution always means reduced toxicity.

II. Products Affected By the Guidance

A. Granular Pesticide Products

For purposes of this guidance, the Agency defines granular pesticide products to include those products composed of less than 10% of a registered active ingredient(s), greater than 90% of List 4 inert carrier(s) (corn cobs, clay, limestone, sand, food) and a minimal amount of sticker/binder (5% or less of the formulation).

If the acute toxicity profile of the registered source product(s) is in Category III or IV for all endpoints, then the proposed pesticide product may use the acute toxicity profile of the registered source product.

In addition, for systemic toxicity (i.e. acute oral, dermal and inhalation) endpoints, it is acceptable to extrapolate Category III data down to Category IV. This extrapolation for acute systemic toxicity is based on dilution. The assumption is that the innocuous inert does not contribute to the toxicity, and thus acts as a diluent. If an extrapolated dose is borderline between two toxicity categories, the Agency will label with the more restrictive toxicity category.

If the primary eye and dermal irritation effects are classified in Category III and/or IV, the

categories of the source registered product may be used for the proposed pesticide product and the toxicity profile will be complete.

EXAMPLE 1:

Source Product Study	Toxicity Category	Toxicity Category for Granular Product
Acute oral LD50	III	IV
Acute dermal LD50	III	IV
Acute inhalation LD50	III	IV
Primary Eye Irritation	III	III
Primary Skin Irritation	III	III
Skin Sensitization	Non-sensitizer	Non-sensitizer

If the acute LD_{50}, dermal LD_{50}, Inhalation LD_{50}, primary dermal and/or eye irritation effects for the registered product(s) are classified in Category I and/or II, then the Agency will not accept calculations that bridge down from these categories and additional data would be required for the proposed pesticide product. Either these studies would need to be submitted, or the registrant would need to cite data on a substantially similar product.

EXAMPLE 2:

Source Product Study	Toxicity Category	Toxicity Category for Granular Product
Acute oral LD50	II	II
Acute dermal LD50	II	II
Acute inhalation LD50	I	I
Primary Eye Irritation	III	III
Primary Skin Irritation	III	III
Skin Sensitization	Non-sensitizer	Non-sensitizer

For dermal sensitization, if a granular product contains <u>any</u> ingredient which is a known sensitizer, the formulated product would be labeled as a sensitizer. If the product is not a dermal sensitizer, and there are no known dermal sensitizers in the product, a dermal sensitization study may be waived and the product will not require sensitization labeling. If dermal sensitization data on a substantially similar product indicates no dermal sensitization at low concentrations, these data may be cited in support of the product. This determination will be made with data on the active ingredient or information provided by the registrant on an inert (e.g., Material Safety Data Sheet - MSDS). If the registrant knows there is a sensitizing component and can justify the finding, the Agency will not require testing.

B. <u>Granular Fertilizer Pesticide Products</u>

For purposes of this guidance, EPA defines granular fertilizer pesticide products to include those products composed of less than 10% of a registered active ingredient(s), greater than 90%

granular fertilizer components plus clearly recognized innocuous (List 4) inert carrier(s), and a minimal amount of sticker/binder (5% or less of the formulation).

The fertilizer components of these products are considered analogous to the innocuous inert described above with the exception of eye irritation. In some cases, fertilizer products are more irritating to the eye than the comparable non-fertilizer granular products. Therefore, the primary eye irritation results may not be bridged under this guidance. A separate eye irritation study is expected to be performed with the pesticide/fertilizer formulation containing the highest free level of nitrogen. If, at some point, the nitrogen content of the fertilizer component is increased above the tested level, a new primary eye irritation study will be required.

III. Exclusions To This PR

Rodenticide baits are not included in this policy. In the Agency's experience, rodenticide baits are often more toxic than would be predicted using the bridging methods outlined above. In general, the Agency will continue to allow similar baits to use one set of data for purposes of precautionary labeling.

IV. What Registrants And Applicants Should Do

The registrant should submit the following information with the application: (1) request in writing that the Agency apply this guidance to their product; (2) the acute toxicity profile (with corresponding MRID Numbers) for the registered product(s); and (3) the current label for the registered product(s). The Agency will use this information to determine an acute toxicity profile for the product.

VI. Non-Binding Statement

This PR Notice provides guidance to EPA and to pesticide registrants. This notice is not binding on either EPA or pesticide registrants, and EPA may depart from the guidance provided in individual circumstances. Likewise. pesticide registrants may assert that the guidance is not appropriate for a specific pesticide or situation.

VI. Additional Information

You may contact:

John Redden
Registration Division (7505C), USEPA
401 M Street, SW
Washington, DC 20460
(703) 305-1969
redden.john@epa.gov

James J. Jones, Director
Registration Division