United States Environmental Protection Agency | Office of Prevention, Pesticides And Toxic Substances August (7508W) | EPA-738-R-95-028 February 1996

R.E.D. FACTS

PROMETRYN

Pesticide Reregistration

All pesticides sold or used in the United States must be registered by EPA, based on scientific studies showing that they can be used without posing unreasonable risks to people or the environment. Because of advances in scientific knowledge, the law requires that pesticides which were first registered years ago be reregistered to ensure that they meet today's more stringent standards.

In evaluating pesticides for reregistration, EPA obtains and reviews a complete set of studies from pesticide producers, describing the human health and environmental effects of each pesticide. The Agency imposes any regulatory controls that are needed to effectively manage each pesticide's risks. EPA then reregisters pesticides that can be used without posing undue hazards to human health or the environment.

When a pesticide is eligible for reregistration, EPA announces this and explains why in a Reregistration Eligibility Decision Document, or RED. This fact sheet summarizes the information in the RED document for reregistration case 0467, prometryn.

Use Profile

Prometryn is a substituted thiomethly triazine herbicide registered for the control of several annual grasses and broadleaf weeds in terrestrial food and feed crops cotton, celery, pigeon peas and dill. Prometryn's mechanism of action inhibits the electron transport in target broadleaves and grasses. Prometryn was first registered in 1964 by Ciba Crop Protection. Prometryn is also manufactured by the Verolit Chemical Manufacturer, Ltd. Prometryn's major use sites are cotton and celery.

Other names for prometryn are Prometryne, Caparol, Gesagard, Primatol Q, and Prometex. Prometryn is formulated as a single active ingredient in wettable powder, crystalline, and flowable concentrate. Prometryn is also formulated in a multiple active ingredient product which combines a flowable concentrate with monosodium methanearsonate. Currently there are 17 registered products (includes two Special Local Need registrations) that contain from 8 to 97 percent prometryn. There are no homeowner use products registered.

Regulatory History

Prometryn was first registered in the United States in 1964 as a herbicide for the control of weeds in cotton, celery, pigeon peas, and dill. A Registration Standard was issued in March 1987 (NTIS# PB87-184826), and required product and residue chemistry, toxicology, fish and wildlife, plant protection, and environmental fate data. Additionally, the Special Review and Reregistration Division issued two Data Call-Ins, one September 30, 1991, requesting Tier III non-target phytotoxicity field studies and Spray Drift information, and the second, September 2, 1992, requesting hexachlorobenzene (HCB) and penta-chlorobenzene (PCB) data to determine the potential presence of the impurities in technical prometryn. Lacking appropriate guidance for conducting Tier III testing and because of our new policy, the Agency has decided to assess risk and make reregistration decisions based on Tier II laboratory data. Therefore, the Agency placed Tier III study requirements on reserve. The Reregistration Eligibility Decision document reflects the reassessment of the data submitted in response to the Registration Standard and both Data Call-Ins.

Human Health Assessment

Toxicity

In studies using laboratory animals, prometryn technical has been shown to be slightly to practically non-toxic for oral, dermal, inhalation and has been placed in Tox Category III (next to lowest in the four categories) for these. Additionally, pertaining to acute eye and dermal irritation, prometryn technical is considered to be slight to practically non toxic, respectively and has been categorized as being in Categories III and IV for these. Prometryn is not considered a sentizer.

In a subchronic 28-day feeding study using rats showed that macroscopic and microscopic pathological findings appeared in the high dose animals and were limited to the G.I. tract along with clinical signs and marked decreases in body weights were also seen in these animals. In a 21-day dermal toxicity study with rabbits, no local or systemic toxicity was observed at the highest dose levels (1000 mg/kg/day).

In three chronic toxicity/carcinogenicity studies with mice, rats and dogs showed that prometryn was not oncogenic. Prometryn was classified as a Group E Carcinogen (no evidence of human carcinogenic potential) because prometryn did not alter the spontaneous tumor profile for the strains of mice and rats tested. The dog study, however, was not considered because, even though there were some effects, under the conditions of the study, the effects were not oncogenic.

A developmental toxicity study with rats showed the highest dose level caused maternal and developmental toxicity. In another study also conducted with rabbits resulted in effects at the highest dose level, including increased abortions and decrease in body weight parameters.

A 2-generation reproductive study with rats showed effects at the highest dose level including decrease in body weight and corresponding food consumption. Nevertheless, the statistically significant decrease in pup body weight (also at the high dose level) was considered to be toxicologically significant because of its potential negative impact on post-natally developing systems such as the neuro- and immune systems.

In four mutagenicity studies (ames samonella test, chromosomal aberration, bacterial DNA repair, and unscheduled DNA synthesis test) prometryn was found to be negative.

A series of (radiolabeled) general metabolism studies with rats showed the greatest distribution of prometryn first in the blood followed by the spleen and then in the lungs.

Dietary Exposure

People may be exposed to residues of prometryn through the diet. Tolerances or maximum residue limits have been established for a variety of crop and animal commodities (see 40 CFR 180.222(a) and (b)).

Food and Feed additive tolerances are established for residues of prometryn in or on the following raw agricultural commodities: celery (0.5 ppm); corn fodder (field, pop, and sweet, 0.25 ppm); corn forage (field, pop, and sweet, 0.25 ppm); fresh corn (sweet K +CWHR, 0.25 ppm); corn grain (0.25 ppm); cotton[forage](1 ppm); cottonseed (0.25 ppm); and pigeon peas (0.25 ppm). A tolerance with regional registration is established in or on dill (0.03 ppm).

The Agency has determined that a risk assessment for the uses of prometryn can be conducted using tolerance-level residues of prometryn, per se in cottonseed, pigeon peas, celery and dill.

The Agency has assessed the dietary risk posed by prometryn considering tolerance level residues to calculate the Theoretical Maximum Contribution (TMRC) for the overall US population and 22 subgroups. No refinements using anticipated residues or percent crop treated were applied. Two analysis were conducted, one included the commodity (corn) for which revocation of tolerance is recommended and the other did not include the proposed revocation of tolerances on corn. Both chronic analyses indicated a negligible chronic dietary risk from the use of prometryn.

The RfD was determined to be 0.04 mg/kg/day based on a NOEL of 3.75 mg/ kg/day from a chronic toxicity study in dogs. The LEL was determined to be 3.75 mg/kg/day based on bone marrow atrophy and degenerative changes in the liver and kidneys. An uncertainty factor of 100 was used to account for inter- and intra- species variability.

An acute dietary analysis has been recommended. The endpoint for acute dietary risk assessment is the NOEL of 12 mg/kg/day from a rabbit

developmental study, while the LEL was based on increased resorptions, abortion and significant changes in other reproductive parameters at 72 mg/kg body weight/day.

Occupational Exposure

Based on current use patterns, handlers (mixers, loaders, and applicators) may be exposed to prometryn during and after application in agricultural settings. There are no data to evaluate post-application exposure because post-application data were not required in the Registration Standard and subsequent DCI's, because at the time no toxicological criteria had been triggered. There are no residential uses for prometryn and no exposure risk is expected to homeowners.

There are toxicological endpoints of concern for prometryn. The endpoint for both short-term and intermediate-term occupational exposure is a NOEL of 12 mg/kg/day taken from a rabbit developmental study indicating increased resorption, abortion, and significant changes in other reproductive parameters at the LEL. The LEL is 72 mg/kg/day and the Agency deemed a 15% factor appropriate for estimating dermal exposure.

Although no dermal absorption study with prometryn was ever conducted, the Agency determined that a 7% absorption value is a reasonable upper limit for dermal absorption. The 7% is based on a comparison between an oral rabbit developmental study and a 21-day dermal rabbit study. However, uncertainties and concerns exist regarding the use of 7% in conducting the risk assessment because the parameters typically measured in a 21-day dermal study are not extensive (i.e., no clinical chemistries) and the effects observed including increased abortion and increased post-implantation loss in the developmental study are significant . Thus, the Agency has decided to use a more protective absorption rate of 15%.

The Agency has determined that there is an exposure potential for handlers during the usual use-patterns associated with prometryn. Exposures to mixers, loaders and applicators are likely when liquid (used in aerial application) and wettable powder (used in aerial and groundboom applications) formulations are used. In the same manner, the Agency has determined that there is a potential for exposure to persons entering treated sites after application is complete with special concern for lay-by applications to celery, since such applications can be made over the crop and celery is often thinned by hand.

Human Risk Assessment

To mitigate the risks posed to handlers, the Agency is requiring that all wettable powder formulations be encased in soluble packets. To mitigate the risks associated with mixing and loading liquid formulations to support aerial applications, the Agency is requiring minimum (baseline) PPE of a chemical resistent apron and a respirator equipped with a dust/mist

filter. Additionally, to protect field workers, the Agency is requiring a 24-hour REI for uses on celery and a 12-hour REI for all other uses. The Agency is also requiring interim spray drift advisory measures be placed on all labels, and is requiring a confirmatory post-application/ reentry study for celery to assess the impact posed to reentry workers.

Environmental Assessment

Environmental Fate

The laboratory mobility data for prometryn indicate that prometryn has the potential to leach into ground water and will be most mobile in sandy, alkaline soils which contain little organic matter or clay. Prometryn was detected in ground water from an irrigation well in California. However, in California, Arizona and New Mexico, prometryn labels instruct potential users not to apply the product to sand or loamy sand soils. Also, prometryn was not detected in ground water during a retrospective ground-water monitoring study performed by the registrant in Missouri, at a site which was underlain by sandy loams and loamy sands.

Ecological Effects

Because prometryn is registered for the control of weeds in terrestrial feed and food crops; cotton, celery, pigeon peas and dill, it is expected that exposure to nontarget organisms can result from direct applications, spray drift, and runoff from treated areas. Studies indicate that prometryn poses an acute risk to nonendagered and endangered terrestrial and aquatic plants, a chronic risk to birds, and an acute risk to endangered small mammals.

Prometryn is currently not classified as a restricted use pesticide. Although the restricted use risk quotients are at the threshold for small mammals, fresh water invertebrates and estuarine/marine organisms, the Agency has determined that the numbers do not warrant the chemical's reclassification at this time.

Ecological Effects Risk Assessment

The Agency is requiring labelling prohibiting the use of prometryn on sand and sandy loam soils. However, in light of the registrant's stewardship and the data-in-house, the Agency has determined that ground water and surface water label advisories are not necessary at this time.

All of the ecological effects data required are fulfilled with the exception of an avian reproduction (upland gamebird) study and a fish early life stage study. These studies are needed to fully assess prometryn's risk assessment to birds and fish.

In order that the use of prometryn will not endanger sensitive terrestrial and aquatic plant species and to reduce potential risks, the Agency is requiring all products to carry environmental hazard labeling. Additionally, in the future, when the Agency implements the Endangered

Species Protection Program, limitations may be imposed on the use of prometryn to protect threatened and endangered species.

Additional Data Required

The Agency is requiring the following generic data for prometryn to confirm its regulatory assessment and conclusions:

- o Guideline 71-4(a) Avian reproduction (upland gamebird)
- o Guideline 72-4(a) Fish early life-stage
- o Guideline 85-2 Dermal absorption
- o A confirmatory post-application/reentry study for celery. The study shall consist of:
  - Guideline 132-1(a) Foliar dislodgeable residue dissipation,
  - Guideline 132-1(b) Soil residue dissipation, and
  - Guideline 133-3 Dermal exposure to be conducted concurrently.
- o Guideline 165-2 Limited field rotational crop study (for leafy vegetables).

Additionally, the Agency is requiring product-specific data including product chemistry and acute toxicity studies, revised Confidential Statements of Formula (CSFs), and revised labeling for reregistration.

Product Labeling Changes Required

The labels of all registered pesticide products containing prometryn must comply with the Agency's current pesticide labeling requirement and with the additional requirements summarized below.

Worker Protection Requirements

Personal Protective Equipment (PPE) Requirements

For Occupational Use

The minimum (baseline) PPE for all prometryn occupational handlers of prometryn end-use products is:

"Applicators and other handlers must wear:

-- long sleeve shirt and long pants,

-- Chemical resistant gloves, and

-- Shoes plus socks."

For the liquid-formulation end-use products that contain instructions for aerial applications, the Agency is requiring the following additional minimum (Baseline) PPE for mixers and loaders supporting aerial application:

"In addition, mixers and loaders supporting aerial applications must wear:

-- Chemical resistant apron, and

-- Respirator (a dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC-21C)).

Entry Restictions

For Occupational-Use

A 24-hour restricted entry interval (REI) is required for celery and a 12-hour (REI) is required for all other uses. The PPE required for early entry is:

--Coveralls over long-sleeve shirt and long pants,

--Chemical-resistant gloves,

--Shoes plus socks.

Other Labeling Requirements

For Occupational Use:

"Do not apply this product in a way that will make contact with workers or other persons, either directly or through drift. Only protected handlers may be in the area during application."

Engeneering Controls:

"When handlers use closed systems (including water-soluble packets), enclosed cabs, or aircraft in a manner that meets the requirements listd in the Worker Protection Standard (WPS) for agricultural pesticides (40 CFR 170.240(d)(4-6), the handler PPE requirements may be reduced or modified as specified in the WPS."

User Safety Requirements:

"Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry."

User Safety Recommendations:

- "Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet."
- "Users should remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing."
- "Users should remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing."

Soil Incorporation Statement

Registrants may add the following statement to their labeling in the Agricultural Use Requirements box immediately following the restricted entry interval:

"Exception: If the product is soil-incorporated, the Worker Protection Standard, under certain circumstances, allows workers to enter the treated area if there will be no contact with anything that has been treated."

Environmental Hazard:

For all prometryn end-use products, use this precautionary statement:

"Do not apply directly to water or to areas where the surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water when disposing of equipment washwater or rinsate. Drift and runoff may be hazardous to aquatic organisms in neighboring areas. Do not apply where runoff is likely to occur. Do not apply when weather conditions favor drift from treated areas."

Rotational Crops:

Labels must specify a plant-back-interval (PBI) of 8 months for rotational crops.

Spray Drift Label Advisory:

For prometryn products that can be applied aerially, the following statement must be placed on each label:

"Avoiding spray drift at the application site is the responsibility of the applicator. The interaction of many equipment-and-weather-related factors determine the potential for spray drift. The applicator and the grower are responsible for considering all these factors when making spraying decisions."

The following drift management requirements must be followed to avoid off-target drift movement from aerial applications to agricultural crops. These requirements do not apply to forestry applications, public health uses or to applications dry formulations:

1. "The distance of the outer most nozzles on the boom must not exceed 3/4 the lenght of the wingspan or rotor."
2. "Nozzles must always point backward parallel with the air stream and never be pointed downwards mure than 45 degrees."

Where states have more stringent regulations, they should be observed.

The applicator should be familiar with and take into account the information covered in the Aerial Drift Reduction Advisory Information.

The following aerial drift reduction advisory information must be contained in the product labeling:

[This section is advisory in nature and does not supersede the mandatory label requirements.]

Information on droplet size

The most effective way to reduce drift potential is to apply large droplets. The best drift management strategy is to apply the largest droplets that provide sufficient coverage and control. Applying larger

droplets reduces drift potential, but will not prevent drift if applications are made improperly, or under unfavorable environmental conditions (see Wind, Temperature and Humidity, and Temperature Inversions).

Controlling Droplet Size

- Volume - Use high flow rae nozzles to apply the highest practical spray volume. Nozzles with higher rated flows produce larger droplets.
- Pressure - Do not exceed the nozzle manufacturer's recommended pressures. For many nozzle types lower pressure produces larger droplets. When higher flow rates are needed, use higher flow rate nozzles instead of increasing pressure.
- Number of nozzles - Use the minimum number of nozzles that provide uniform coverage.
- Nozzle orientation - Orienting nozzles so that the spray is released parallel to the airstream produces larger droplets than other orientations and is the recommended practice. Significant deflection from horizontal will reduce droplet size and increase drift potential .
- Nozzle type - Use a nozzle type that is designed for the intended application. With most nozzle types, narrower spray angles produce larger droplets. Consider using low-drift nozzles. Solid stream nozzles oriented straight back produce the largest droplets and the lowest drift.

Boom Length

For some use patterns, reducing the efffective boom length to less than 3/4 of the wingspan or rotor length may further reduce drift without reducing swath width.

Application Height

Applications should not be made at a height greater than 10 feet above the top of the largest plants unless a greater height is required for aircraft safety. Making applications at the lowest height that is safe reduces exposure of droplets to evaporation and wind.

Swath Adjustment

When applications are made with a crosswind, the swath will be displaced downward. Therefore, on the up and downwind edges of the field, the applicator must compensate for this displacement by adjusting the path of the aircraft upwind. Swath adjustment distance should increase, with increasing drift potential (higher wind, smaller drops, etc.).

Wind

Drift potential is lowest between wind speeds of 2-10 mph. However, many factors, including droplet size and equipment type determine drift potential at any given speed. Application should be avoided below 2 mph due to variable wind direction and high inversion potential. NOTE: Local terrain can influence wind patterns. Every applicator should be familiar with local wind patterns and how they affect spray drift.

Temperature and Humidity

When making applications in low relative humidity, set up equipment to produce larger droplets to compensate for evaporation. Droplet evaporation is most severe when conditions are both hot and dry.

Temperature Inversions

Applications should not occur during a temperature inversion because drift potential is high. Temperature inversions restrict vertical air mixing, which causes small suspended droplets to remain in a concentrated cloud. This cloud can move in unpredictable directions due to the light variable winds common during inversions. Temperature inversions are characterized by increasing temperatures with altitude and are common on nights with limited cloud cover and light to no wind. They begin to form as the sun sets and often continue into the morning. Their presence can be indicated by ground fog; however, if fog is not present, inversions can also be identified by the movement of smoke from a ground source or an aircraft smoke generator. Smoke that layers and moves laterally in a concentrated cloud (under low wind conditions) indicates an inversion, while smoke that moves upward and rapidly dissipates indicates good vertical air mixing.

Sensitive Areas

The pesticide should only be applied when the potential for drift to adjacent sensitive areas (e.g. residential areas, bodies of water, known habitat for threatened or endangered species, non-target crops) is minimal (e.g. when wind is blowing away from the sensitive areas).

Regulatory Conclusion

The use of currently registered products containing prometryn in accordance with approved labeling will not pose unreasonable risks or adverse effects to humans or the environment. Therefore, all uses of these products abiding to the requirements imposed in the RED document are eligible for reregistration.

Prometryn products will be reregistered once the required product specific data, revised Confidential Statements of Formula, and revised labeling are received and accepted by EPA.

For More Information

EPA is requesting public comments on the Reregistration Eligibility Decision Document (RED) for prometryn during a 60-day time period, as announced in a Notice of Availability published in the Federal Register. To obtain a copy of the RED or to submit written comments, please contact the Pesticide Docket, Public Response and Program Resources Branch, Field Operations Division (H-7506C), Office of Pesticide Programs (OPP), US EPA, Washington, DC 20460. Telephone 703-305-5805.

Following the comment period, the prometryn RED will be available from the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22161, telephone 703-487-4650.

For more information about prometryn or about EPA's pesticide reregistration program, please contact the Special Review and Reregistration Division (H-7508W), OPP, US EPA, Washington, DC 20460, telephone 703-308-8000. For information about reregistration of individual products containing prometryn, please contact Robert Taylor, Product Manager, Registration Division (H-7505C), OPP, US EPA, Washington, DC 20460, telephone 703-305-6800.