



R.E.D. FACTS

Pesticide Reregistration

Ethephon

All pesticides sold or distributed 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 unreasonable risks to human health or the environment.

When a pesticide is eligible for reregistration, EPA announces this and explains why in a Reregistration Eligibility Decision (RED) document. This fact sheet summarizes the information in the RED document for reregistration case 0382, Ethephon.

Use Profile

Ethephon is a plant growth regulator used to promote fruit ripening, abscission, flower induction, and other responses. Ethephon is registered for use on a number of food, feed and nonfood crops, greenhouse nursery stock, and outdoor residential ornamental plants, but is used primarily on cotton. Formulations include formulation intermediates and soluble concentrates/liquids. Ethephon is applied to plant foliage by either ground or aerial equipment. It also may be applied by hand sprayer to certain home garden vegetables and ornamentals.

Use practice limitations include prohibitions against applying ethephon through any type of irrigation system; feeding or grazing livestock in treated areas; and treating within 2 to 60 days of harvest, depending on the crop.

Regulatory History

Ethephon was discovered in 1965, and was first registered as a pesticide in the U.S. in 1973. EPA issued a Registration Standard for ethephon in September 1988 (PB89-109427), requiring toxicology, residue chemistry, and environmental fate and effects data.

Human Health Assessment

Toxicity

Ethephon is corrosive in acute dermal irritation studies using rabbits, has the potential to cause eye irritation, and has been placed in Toxicity Category I (the highest of four categories) for these effects. It is moderately acutely toxic by the oral, dermal and inhalation routes (Toxicity Category III), and does not cause skin sensitization.

An organophosphate pesticide, ethephon caused plasma cholinesterase inhibition in a 16-day oral human study and clinical signs of toxicity in a second study. In a dermal toxicity study using rabbits, skin effects were observed at all doses.

In a combined chronic/oncogenicity study using rats, plasma and erythrocyte cholinesterase were inhibited at all doses. At the highest dose levels, ethephon caused body weight decrease and kidney effects, but no carcinogenic effects were observed. In a cancer study using mice, no evidence of treatment related tumors was observed. Ethephon has been classified as a Group D carcinogen based on "the insufficiency of the weight of evidence" regarding its cancer-causing potential.

One chronic toxicity study using beagle dogs caused plasma cholinesterase inhibition at all doses, and smooth muscle atrophy in the gut. In a second beagle dog study, treatment related effects included decreased spleen and body weight plus decreased hemoglobin and hematocrit in the males.

Developmental toxicity studies using rats and rabbits show no evidence of a potential for developmental effects at doses that are not toxic to the mother. In a reproductive toxicity study using rats, administration of the test compound caused decreased survival in the offspring and decreased body weight gain in adult females, but no effects on fertility, gestation, mating, organ weights, or histopathology in any generation.

Ethephon was positive in one mutagenicity study and negative in two others. It does not appear to cause delayed neurotoxicity based on a study using hens, however studies using mammals are now required as confirmatory data.

Human poisoning incidents involving ethephon include four cases of skin injury (irritation) in California as a result of exposure to field residues, one possible systemic poisoning case, and 29 telephone calls to the National Pesticides Telecommunications Network reporting eye and skin irritation from misuse of ethephon, sometimes in combination with other pesticides.

Dietary Exposure

People may be exposed to residues of ethephon through the diet. Tolerances or maximum residue limits have been established for ethephon in many raw agricultural commodities, processed foods, and feed. Please see 40 CFR 180.300(a) and (b), 185.2700(a), (b) and (c), and 186.2700(a).

Several additional tolerances, including food and feed additive tolerances, have been proposed.

Sufficient data are available to assess the adequacy of most established ethephon tolerances, although some require additional residue chemistry or animal feeding studies. Some changes are needed; certain tolerances must be revoked because registrations for these crop uses no longer exist, and a tolerance for cottonseed must be increased. Several new tolerances may need to be established.

EPA has assessed the chronic dietary risk posed by ethephon, evaluating exposure and risk, first, from all uses for which tolerances exist, have been recommended or have been proposed and, second, excluding uses for which revocation is recommended. For the overall U.S. population and 22 subgroups, the Anticipated Residue Contribution (ARC) from all current and proposed ethephon tolerances represents 9% of the Reference Dose (RfD), an amount believed not to cause adverse effects if consumed daily over a 70-year lifetime. The ARC of the most highly exposed subgroup, non-nursing infants less than one year old, represents 49% of the RfD. Excluding the tolerances recommended for revocation, the ARC for the overall U.S. population represents 8.6% of the RfD, while the ARC for non-nursing infants represents 47% of the RfD. Therefore, it appears that chronic dietary risk is not of concern.

Because ethephon causes neurotoxic effects (cholinesterase inhibition), an acute dietary exposure analysis also was conducted. Margins of Exposure (MOEs), which show how closely estimated exposure comes to a dose of concern, were calculated for several population subgroups. Infants less than one year old are the only subgroup whose exposure may be of concern, with 5% of the population estimated to have MOEs of less than 7 (an MOE of 10 or greater is desirable). However, these risk values represent an unrealistic worst case situation. Many conservative assumptions were included in calculating these risks, such as: all registered food crops are treated; maximum residue levels are present on all foods; and no dilution or degradation of residues has occurred during preparation or processing of food. EPA believes it is unlikely that infants and children will be exposed to ethephon-treated commodities at levels that will result in acute dietary risk.

Several international Codex Maximum Residue Limits (MRLs) have been established for ethephon. Compatibility between U.S. tolerances and Codex MRLs exists for apples, blackberries, cherries, pineapples and walnuts, and may be achieved for tomatoes by raising the U.S. tolerance. For other crops, the U.S. tolerances are being revoked or additional field residue data are needed.

Occupational and Residential Exposure

Based on current use patterns, workers may be exposed to ethephon in agricultural and other settings, during and after applications using open pouring methods and broadcast (aerial and ground) treatment or hand-held spray equipment. Ethephon does not pose risks of systemic dermal or inhalation toxicity. However, since it does pose risks of severe skin and eye irritation (Toxicity Category I), certain Worker Protection Standard (WPS) provisions apply.

To protect post-application workers, a 48-hour restricted entry interval (REI) imposed by the WPS is being retained. This interval must be increased to 72 hours when ethephon is applied outdoors in arid areas. Certain personal protective equipment (PPE), including protective eyewear, is required for early entry into treated areas. In addition, since ethephon is in Toxicity Category I for primary skin irritation, "double notification" is required: agricultural workers must be warned orally of its application, **and** WPS warning signs must be posted at entrances to treated areas.

Human Risk Assessment

Ethephon has the potential to cause severe skin and eye irritation (Toxicity Category I), but otherwise is moderately acutely toxic. An organophosphate pesticide, it has the potential to cause cholinesterase inhibition. Ethephon is classified as a "Group D" carcinogen because there is insufficient weight of evidence regarding its cancer-causing potential.

Ethephon is used on many food and feed crops. Its tolerances have been reassessed, and while they generally are acceptable, some changes are required. EPA's dietary risk assessments indicate that infants less than one year old encounter the greatest exposure and risk as a result of ethephon crop use. However, since the Agency used many conservative assumptions in calculating these risks, actual dietary exposure and risk to infants as well as the overall U.S. population are believed to be minimal.

Pesticide handlers may be exposed to ethephon during application, and post-application workers may be exposed to residues on treated crops. To reduce workers' skin and eye irritation risks, a 48-hour REI is being retained and is increased to 72 hours in arid areas, use of certain PPE including protective eyewear is required for early entry, and double notification of workers is required.

Environmental Assessment

Environmental Fate

Ethephon is not persistent in the environment. The major routes of dissipation appear to be chemical hydrolysis and microbial degradation. Although ethephon degrades in somewhat acidic soils (pH 6.1), it does not hydrolyze in sterile, acidic water (pH 5). The major degradates are ethylene gas and 2-hydroxy ethyl phosphonic acid. Ethephon has moderate to low mobility in soil. It has a very low octanol/water partition coefficient and, therefore, is not expected to accumulate in fish.

In the field, ethephon exhibits the same characteristics of rapid degradation and moderate to low mobility as seen in the laboratory. At field sites in southern California, North Carolina, and Washington, ethephon dissipated with half-lives of about 7 to 25 days.

Ecological Effects

In dietary studies using the bobwhite quail and mallard duck, ethephon is practically nontoxic to slightly toxic on an acute basis, and practically nontoxic on a subacute basis. Acute oral studies using rats show that ethephon is slightly toxic to mammals. Other acute toxicity studies show that ethephon is practically nontoxic to coldwater fish, and practically nontoxic to slightly toxic to warmwater fish and freshwater invertebrates. Ethephon is practically nontoxic to shrimp, and slightly toxic to estuarine/marine mollusks. It is relatively nontoxic to honeybees. Regarding effects on terrestrial plants, ethephon reduces plant growth, resulting in reduced shoot lengths and weights.

Ecological Effects Risk Assessment

Ethephon is expected to have minimal effects on birds and mammals, as well as on fish, freshwater invertebrates, and marine and estuarine organisms.

Although minimal effects to aquatic and terrestrial plants (dry land) are expected, ethephon may pose a risk to semi-aquatic/wetland plants (including endangered semi-aquatic plants) when it is used on apples in North Carolina, cotton, tobacco, macadamia nuts, blackberries and pineapple. However, ethephon is a growth regulator and as such is not intended to be toxic to plants. Also, the magnitude of this risk is not high. Therefore, while the potential for risk to semi-aquatic plants exists, it is not extensive, arises only infrequently during periods of high exposure, and is geographically limited.

In response to Agency concerns about ethephon's risk to semi-aquatic plants, the registrant proposed as a risk mitigation measure to reduce the maximum use rate for blackberries and apples in North Carolina to 2.0 pounds per acre. They also provided information indicating that ethephon is used only occasionally at maximum rates when certain weather conditions exist, such as cool temperatures. Considering these factors, EPA believes that the risk to nontarget plants from use of ethephon will be limited.

Additional Data Required

EPA is requiring the following additional generic data for ethephon to confirm its regulatory assessments and conclusions: Product chemistry; Animal metabolism (poultry); Residue analytical method in plants and animals; Storage stability; Magnitude of the residue in plants (peppers, cantaloupes, grapes, wheat forage and hay, and cotton gin byproducts); Magnitude of the residue in processed sugarcane; Magnitude of the residue in poultry and ruminant; Batch equilibrium on the degradate of 2-hydroxy ethyl phosphonic acid; Acute and subchronic neurotoxicity.

The Agency also 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

All ethephon end-use products must comply with EPA's current pesticide product labeling requirements, and with the following:

Worker Protection

Personal Protective Equipment (PPE) for Handlers

PPE for handlers will be based on the toxicity of each end-use product (see PR Notice 93-7). If PPE is necessary for homeowner uses, it will be established during end-use product reregistration.

Entry Restrictions for Occupational-Use Products:

Worker Protection Standard (WPS) Uses

EPA is establishing a 48-hour restricted entry interval (REI), which increases to 72 hours in outdoor areas where average rainfall is less than 25 inches a year. PPE for WPS-permitted early entry into treated areas is coveralls over long-sleeved shirt and long pants, chemical-resistant gloves such as any waterproof gloves, chemical-resistant footwear plus socks, and chemical-resistant headgear for overhead exposures. In addition, protective eyewear is required since ethephon is in Toxicity Category I for eye irritation potential.

Non-WPS Uses

Products with uses outside the scope of the WPS must bear the following statement:

"Do not allow people or pets to touch treated plants until the sprays have dried."

Entry Restrictions for Homeowner-Use Products

Ethephon products with directions for use by homeowners must bear the following statement:

"Do not allow people or pets to touch treated plants until the sprays have dried."

Other Labeling Requirements

Reduce PPE when Engineering Controls are Used

"When handlers use closed systems, enclosed cabs, or aircraft in a manner that meets the requirements listed in the WPS [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 exist for washables, use detergent and hot water. Keep and wash PPE separately from other laundry."

"Discard clothing and other absorbent materials that have been drenched or heavily contaminated with this product's concentrate. Do not reuse them."

User Safety Statements

"Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet."

"Users should remove clothing immediately if pesticide gets inside."

"Users should remove PPE immediately after handling this product. As soon as possible, wash thoroughly and change into clean clothing. Wash the outside of gloves before removing."

Application Restrictions

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

Notification

"Notify workers of the application by warning them orally and by posting warning signs at entrances to treated areas."

Environmental Hazard

The following precautionary statement is required to address risks to wetlands:

"Do not apply directly to water, or to areas where surface water is present, or to intertidal areas below the mean high water mark."

For residential use sites (ornamental trees, shrubs, vines and herbaceous plants), the statement, "Do not apply directly to water" may be used instead of the statement above.

Spray Drift

The following language is required on each product label that can be applied aerially:

"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 is responsible for considering all these factors when making decisions."

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

"1. The distance of the outer most nozzles on the boom must not exceed 3/4 the length of the wingspan or rotor."

"2. Nozzles must always point backward parallel with the air stream and never be pointed downwards more 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

- o "Volume - Use high flow rate nozzles to apply the highest practical spray volume. Nozzles with higher rated flows produce larger droplets."
- o "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."
- o "Number of nozzles - Use the minimum number of nozzles that provide uniform coverage."
- o "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."
- o "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 effective 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 target 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 downwind. Therefore, on the up and downwind edges of the field, the applicator should 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 winds 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)."

Residue Chemistry

The following label revisions must be added to pertinent end-use products:

- Product labels must be amended to reflect a maximum allowable use rate of 2 lb ai/A/season for application of ethephon to cotton.
- Label directions for apples, cranberries, carob, and olives that are for ornamental use only must be clearly designated as such.
- The 0.33 lb/gal SC/L label (264-263) must be amended to prohibit the harvesting of any treated pumpkins for human or animal consumption and must specify that treatments are to be made to pumpkins for seed production only.
- Labels must be amended to reduce the maximum use rate for blackberries and apples in N.C. to 2.0 lb per acre.

A table near the end of the RED document identifies the Food/Feed Use Patterns Subject to Reregistration for Ethephon. This table lists currently acceptable use sites, formulations, application rates, methods and equipment, pre-harvest and reentry intervals, and use limitations for ethephon products registered by the basic manufacturer. All ethephon end-use product labels must be amended to be consistent with the basic producer labels, as reflected in this table.

Regulatory Conclusion

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

Ethephon 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 (RED) document for ethephon 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 document or to submit written comments, please contact the Pesticide Docket, Public Response and Program Resources Branch, Field Operations Division (7506C), Office of Pesticide Programs (OPP), US EPA, Washington, DC 20460, telephone 703-305-5805.

Electronic copies of the RED and this fact sheet can be downloaded from the Pesticide Special Review and Reregistration Information System at 703-308-7224. They also can be reached on the Internet via *FEDWORLD.GOV*, or obtained from EPA's gopher server, *EARTH1.EPA.GOV*.

Printed copies of the RED and fact sheet can be obtained from EPA's National Center for Environmental Publications and Information (EPA/NCEPI), PO Box 42419, Cincinnati, OH 45242-0419, telephone 513-489-8190, fax 513-489-8695.

Following the comment period, the ethephon RED document also 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 EPA's pesticide reregistration program, the ethephon RED, or reregistration of individual products containing ethephon, please contact the Special Review and Reregistration Division (7508W), OPP, US EPA, Washington, DC 20460, telephone 703-308-8000.

For information about the health effects of pesticides, or for assistance in recognizing and managing pesticide poisoning symptoms, please contact the National Pesticides Telecommunications Network (NPTN). Call toll-free 1-800-858-7378, between 8:00 am and 6:00 pm Central Time, Monday through Friday.