United States Environmental Protection Agency | Prevention, Pesticides And Toxic Substances (7508W) | EPA-738-F-96-005 December 1995

R.E.D. FACTS

Gibberellic Acid

Pesticide Reregistration

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 before November 1, 1984, 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 develops mitigation measures or regulatory controls needed to effectively reduce 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 explains the basis for its decision in a Reregistration Eligibility Decision (RED) document. This fact sheet summarizes the information in the RED document for reregistration case number 4110, Gibberellic Acid.

Use Profile

For the purpose of this RED, the following compounds will be considered collectively under the term "Gibberellic Acids": Gibberellic Acid (GA_3); related isomers known as Gibberellins ($GA_4 + GA_7$); and the salt of the acid, Potassium Gibberellate.

Gibberellic Acids are naturally occurring plant hormones. Gibberellic Acids are used in agriculture as plant regulators to stimulate both cell division and cell elongation that affect leaves as well as stems (eventually affecting fruit development and fruit set). Applications of Gibberellic Acids can also hasten plant maturation and seed germination. Because they are naturally occurring compounds and have a nontoxic mode of action in target plants, Gibberellic Acid and related isomers have been classified as biochemical pesticides.

Gibberellic Acids are applied to growing crops (field crops, small fruits, vines and tree fruits), ornamental and shade tress, and ornamental plants, shrubs and vines. The Agency has determined that the uses of Gibberellic Acids, as currently registered, will not cause unreasonable risk to humans or the environment. These uses are eligible for reregistration. However, six of the uses currently on the labels are not covered by either the exemption from tolerance (40 CFR 180.1098), or a numeric tolerance

(40 CFR 180.224). The Agency plans to propose to exempt from tolerance many plant regulators, including Gibberellic Acids, when used in low doses. This exemption will apply only when application rates do not exceed 250 grams of ai/acre/year. The Agency believes this action does not present unreasonable risks because it is based on Gibberellic Acid's low acute mammalian toxicity, low use rates, naturally occurring exposure in the diet from numerous plant sources, and minimal exposure in the diet derived from consumption of treated commodities under the proposed maximum label use rate.

Formulation Types Registered:

Formulations include tablets, soluble granules, and liquid concentrate.

Method and Rates of Application:

Gibberellic Acid (GA_3) and Gibberellin Mixture ($GA_4 + GA_7$):

Gibberellic Acid (GA_3) and Gibberellin Mixtures ($GA_4 + GA_7$) may be applied by aircraft, irrigation systems, ground spray equipment, seed treatment or soil incorporation.

Potassium Gibberellate:

Potassium Gibberellate may be applied by hand-held spray equipment and as a seed treatment.

Use Practice Limitations

For terrestrial uses:

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

"Do not apply through any type of irrigation system."

Regulatory History

The plant regulator, Gibberellic Acid, was initially registered in the United States in 1947 as PROVIDE GROWTH REGULATOR SOLUTION (EPA Reg. No. 275-2) for applications to apple trees as a means of controlling fruit russet fungus. Gibberellic Acids are naturally occurring plant hormones that act as plant regulators, promoting cell division and cell elongation leading to increased fruit set and crop yields.

During Phase 4 of the accelerated pesticide reregistration process, the data base for Gibberellic Acids was evaluated and determined to be inadequate in satisfying certain requirements for biochemical pesticides, which include plant growth regulators. A DCI was issued in September 1993 to fill the outstanding data gaps.

The biochemical data requirements for the reregistration of Gibberellic Acids have been satisfied through the submission of data in response to the 1993 DCI. These data are adequate to support the registration of Gibberellic Acids on all RAC's, as well as all of the currently registered uses.

Human Health Assessment

Toxicity

In studies using laboratory animals, Gibberellic Acids generally have been shown to be of low acute toxicity. The acute dermal toxicity (LD_{50} > 2g/kg), acute inhalation (negative LC_{50} at 2.98mg/l and LC_{50} > 5.9mg/l), eye irritation (all cleared in 7 days) place Gibberellic Acids in Toxicity Category III (the second lowest of four toxicity categories). Gibberellic Acids acute toxicity (LD_{50} > 5g/kg), dermal irritation (mild to slight), and dermal sensitization (mild sensitizer) place it in Toxicity Category IV (the lowest of four toxicity categories).

[NOTE: For acute oral, dietary, mammalian/avian/aquatic toxicity:
Category I = very highly or highly toxic
Category II = moderately toxic
Category III = slightly toxic
Category IV = practically non-toxic]

Subchronic Toxicity

Two subchronic oral toxicity studies for Gibberellic Acids were reviewed in connection with the RED process. In the first subchronic dietary study there was a NOEL of 10,000 ppm and a LOEL of 50,000 ppm based on the occurrence of soft stools in both sexes of rats and increased BUN levels, liver and kidney weights in females. In the second study, there was a NOEL of 10,000 ppm and a LOEL of 25,000 ppm based on alterations in clinical chemistry, decreased food consumption, decreased body weights, increases in relative organ weights (brain, kidney, testis) and gross histopathological changes in the kidney.

Developmental Toxicity

Two developmental toxicity studies for Gibberellic Acids were reviewed for this RED. In the first study, rats were dosed at 0, 100, or 1,000 mg/kg/day for 8 weeks without significant chemical, hematological or pathologic evidence of toxicity. The maternal toxicity NOEL was greater than 1,000 mg/kg/day (HTD). In the second study, rabbits were dosed at 0, 300, or 1,000 mg/kg/day; the highest concentration caused increased mortality, abortion rates, clinical signs of toxicity, and gross pathological observations. The maternal and developmental NOELs were established at 300 mg/kg/day.

Mutagenicity

Gibberellic Acid (GA_3) Salmonella typhimurium test strains TA 98, TA 100, TA 1535, TA 1537, and TA 1538 at concentrations ranging from 0 to 10,000 ug/plate with negative test results up to limit dose of 5,000 and 10,000 ug/plate. The mutagenicity of Gibberellins ($GA_4 + GA_7$) was tested in an Ames assay with *Salmonella typhimurium* test strains TA 98, TA 100, TA 1535, TA 1537, and TA 1538 at concentrations ranging from 0 to 10,000 ug/plate. Test results were negative up to 10,000 ug/plate in the standard set of five histidine negative strains of *Salmonella typhimurium* LT2.

A mouse-micronucleus assay on Gibberellins ($GA_4 + GA_7$) indicated that no increased incidence of micronucleated-polychromatic erythrocytes (m-PCE) were found at levels up to 1200 mg/kg.

An unscheduled DNA synthesis in rat hepatocytes conducted with Gibberellins technical 90% ($GA_4 + GA_7$) was negative for induction of UDS up to 1260 ug/ml, the limit of solubility (MRID 40261603). A second unscheduled DNA synthesis in rat hepatocytes conducted with Gibberellins also was negative.

Dietary Exposure

People may be exposed to residues of Gibberellic Acids through the diet. Tolerances or maximum residue limits have been established for Gibberellic Acid (GA_3) and Gibberellins ($GA_4 + GA_7$)for the following commodities (refer to 40 CFR 180.224).

Gibberellic Acid (0.15 ppm)		Gibberellin Mixture (0.5 ppm)
Artichokes	Leafy vegetables	Apples
Blueberries	Stone fruits	
Citrus fruits	Sugarcane	
Grapes	Sugarcane fodder	
Hops	Sugarcane forage	

An exemption from the requirement of a tolerance (40 CFR 180.1098) has been established for Gibberellins (specifically GA_3) when used as a plant regulator at less than 20g ai/acre in or on the following RAC's:

Barley	Cucumbers	Oranges	Strawberries
Beans	Grapefruit	Peanuts	Squash
Beets (sugar)	Lemons	Peppers	Sugarcane
Broccoli	Lettuce	Potatoes	Tomatoes
Brussels sprouts	Melons	Rice	Turnips
Cabbage	Mints	Rye	Watercress
Cauliflower	Mustard greens	Sorghum (milo)	Wheat
Corn (all)	Oats	Soybean	
Cotton	Onions	Spinach	

The Agency plans to propose an exemption from the requirements of a tolerance for certain Gibberellic Acids (specifically Gibberellic Acid (GA_3), a mixture of Gibberellins ($GA_4 + GA_7$), and Potassium Gibberellate) for all RAC's when treated with application rates under 250 g ai/acre/year. The Agency believes this action does not present unreasonable risks because it is based on Gibberellic Acids' low mammalian toxicity, low use rates, natural background dietary exposure and minimal exposure in the diet derived from consumption of treated commodities under the proposed use rates.

Occupational and Residential Exposure

Based on the application methods listed on the product labels, the potential for eye, dermal, and inhalation exposure to agricultural workers does exist. However, the lack of acute toxicity (i.e., Gibberellic Acids are in Toxicity Categories III and IV) does not trigger additional requirements for evaluation of worker exposure over the existing precautionary labeling currently required under the provisions of the Worker Protection Standards.

Human Risk Assessment

Since exposures and subsequent risks from Gibberellic Acids are not expected, any potential risks from exposures to treated plants will be mitigated by use of baseline personal protective equipment required by the Worker Protection Standards, supplemented by specific precautionary labeling required by this RED. Post-application reentry workers are required to observe a 12 hour Restricted Entry Interval. Because of Gibberellic Acid's low mammalian toxicity, however it is a candidate for a reduced reentry interval from 12 hours to 4 hours.

Environmental Assessment

Based on a review of all available ecological data, exposure information, and Gibberellic Acids non-toxic mode of action, the Agency expects that applications of Gibberellic Acids will pose minimal risk to nontarget wildlife and fish.

Environmental fate studies for biochemicals are not imposed unless adverse effects are observed in ecological effects data. Since no adverse effects are anticipated, the Agency will not, at this time, impose any environmental fate data requirements for the currently registered uses of Gibberellic Acids.

Additional Data Required

EPA is requiring the a revised Confidential Statement of Formula (CSF) and revised product labeling for reregistration.

Product Labeling Changes Required

The Agency has reexamined the toxicological data base for Gibberellic Acid s and concluded that the current precautionary labeling (i.e., Signal Word , Statement of Practical Treatment, and other label statements associated with mitigating risks) adequately mitigate any risks associated with the use of this plant regulator.

Regulatory Conclusion

Based on the reviews of the generic data for Gibberellic Acid, the Agency has sufficient information on health effect and potential for causing adverse effects to human s or the environment. Therefore, the Agency concludes that the use of currently registered products containing Gibberellic Acids in accordance with approved labeling will not pose unreasonable risks or adverse effects to humans or the environment. Certain uses of Gibberellic Acids that have neither a tolerance or an exemption from tolerance requirements (i.e., food use/commodities not listed in 40 CFR 180.224 or 40 CFR 180.1098) will become eligible for reregistration when the proposed tolerance exemption is issued as a final rule in 1996.

For More Information

EPA is requesting public comments on the Reregistration Eligibility Decision (RED) document for [name] 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 are available on the Internet on EPA's gopher server, *GOPHER.EPA.GOV*, or using ftp on *FTP.EPA.GOV*, or using WWW (World Wide Web) on *WWW.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 Gibberellic Acid 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 Gibberellic Acid RED, or reregistration of individual products containing Gibberellic Acid, please contact the Biopesticides and Pollution Prevention Division (7501W), OPP, US EPA, Washington, DC 20460, telephone 703-308-8712.

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 9:30 am and 7:30 pm Eastern Standard Time, Monday through Friday.