United States Environmental Protection Agency | Prevention, Pesticides And Toxic Substances (7508W) | EPA-738-F-96-023 October 1996

R.E.D. FACTS

Chlorpropham

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 any 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 0271, chlorpropham.

Use Profile

Chlorpropham is a herbicide and plant growth inhibitor used to control mouseear chickweed in spinach and fruiting in ginkgo trees, reduce Botrytis infection in Easter lilies as well as assist in their floral bud removal, and inhibit sprouting in stored potatoes. Formulations include emulsifiable concentrates (36%, 46.5%, and 25% active ingredient), soluble concentrates (49.6%, 78.5%, and 78.4% active ingredient) and a ready-to-use product (78.4% active ingredient).

Chlorpropham is applied by aerosol generator, mist blower, sprayer, low pressure ground boom, and foaming apparatus. Use practice limitations include the following:

- NPDES restrictions;
- a 30 day pre-harvest interval for spinach;
- prohibition of use on seed potatoes;
- prohibition of application through any type of irrigation equipment; and
- ventilation requirements.

Regulatory History

Chlorpropham was registered in the United States in 1962 as a pre-emergence and post-emergence herbicide and as a plant growth regulator. It was originally registered for use on a variety of terrestrial food crops, nonfood crops, and ornamentals to control broadleaf weeds and grasses, and sprouting in stored potatoes. The Agency published an evaluation of existing data and identified data gaps in the December 1987 Guidance for the Reregistration of Pesticide Products Containing Chlorpropham as the Active Ingredient (NTIS #PB88-169917). This Registration Standard required additional data in the areas of product chemistry, residue chemistry, toxicology, ecological effects, and environmental fate. By 1990, the primary registrants had dropped all nationwide uses of chlorpropham except for sprout control on post-harvest stored potatoes. However, an additional 11 registrations for use within a particular county or state (registered under FIFRA Sect. 24(c)) remain today for use on spinach, Easter lilies, and ginkgo trees.

A Data Call-In (DCI) was issued in April of 1994 requiring an analytical method to detect a metabolite of chlorpropham, 4-hydroxychlorpropham-O-sulfonic acid, and a residue study to test for that metabolite in meat and milk. The Agency is considering these data confirmatory to the decisions in the RED document.

Human Health Assessment

Toxicity

In studies using laboratory animals, chlorpropham generally has been shown to be of low acute toxicity. It is slightly toxic by the oral route and has been placed in Toxicity Category III (the second lowest of four categories) for this effect. Chlorpropham is a mild eye and skin irritant, and is practically non-toxic through dermal exposure.

A 21-day dermal study using rabbits produced skin irritation and blood cell changes in both sexes. A 60-week chronic feeding study in beagle dogs resulted in reduced body weight gain, anemia, and changes in thyroid function and structure. In a two-year chronic rat feeding study, survival was not adversely affected by treatment. However, body weight gain was reduced and there was destruction and loss of red blood cells.

Chlorpropham has been evaluated for carcinogenic activity in both the rat and mouse. No treatment-related cancer effects were observed in the study using mice, and the only treatment-related effects in the rat occurred at a dose considered excessive by the Agency. The Agency has classified chlorpropham in Group E (evidence of non-carcinogenicity for humans) under the Agency's cancer classification guidelines.

A developmental study in the rat produced one treatment related fetal effect -- an increased incidence of rudimentary 14th rib. A developmental study with rabbits resulted in increased embryo resorptions and post-implantation loss. A reproductive rat study affected growth and

histopathological changes in the spleen, bone marrow, liver, and kidney. Chlorpropham tested positive in two out of four mutagenicity studies.

Dietary Exposure

People may be exposed to residues of chlorpropham through the diet. Currently, raw agricultural commodity tolerances for chlorpropham on post-harvest potatoes and soybeans are listed under 40 CFR §180.181. Also, interim tolerances for multiple crops are listed under 40 CFR §180.319. The Agency has reassessed the tolerance on post-harvest potatoes and determined that the tolerance value should be lowered from 50 ppm to 30 ppm.

The tolerance for soybeans and many of the interim tolerances will be proposed for revocation because their use sites are no longer supported by any registrant of chlorpropham. It should be noted that revoking these tolerances may impact the importation into the United States of corresponding food items bearing chlorpropham residues. Any interested party who wishes to maintain a chlorpropham residue tolerance for importation purposes in the absence of a registered use should contact the Agency. In general, the Agency requires the same product chemistry and toxicology data to support an import tolerance as are required to support FIFRA registrations. The Agency also requires residue chemistry data representative of growing conditions in the exporting countries.

EPA has assessed the dietary risk posed by chlorpropham. When risk was estimated based on tolerance level residues of 30 ppm on potatoes, the Anticipated Residue Concentration (ARC) for the overall U.S. population represents 42% of the Reference Dose (RfD). The RfD is the amount believed not to cause adverse effects if consumed daily over a 70-year lifetime. Any exposure level less than 100% of the RfD is considered to be an acceptable dietary risk. The most highly exposed subgroup, children 1 to 6 years of age, has an ARC which represents 85% of the RfD. Therefore, it appears that chronic dietary risk is minimal.

Occupational and Residential Exposure

Chlorpropham is not currently registered for residential use. Consequently, Margins of Exposure (MOEs), a ratio of the estimated exposure level to the no observed effect level (NOEL) of 500 mg/kg/day from a 21-day dermal study, were only calculated for occupational handlers of chlorpropham in high exposure potential scenarios.

Human Risk Assessment

Acute dietary exposure is anticipated to be significantly lower than 2.5 mg/kg/day, which is the exposure that would trigger a concern based on effects from the developmental rabbit study. Chronic dietary risk was

assessed and exposure to the general population and all subgroups was less than the RfD.

Although chlorpropham is classified as a group E chemical (evidence of non-carcinogenicity for humans) according to the Agency's cancer classification guidelines, one of its metabolites, 3-chloroaniline, is structurally similar to a known carcinogen, 4-chloroaniline. There are no cancer data available on 3-chloroaniline. However, the Agency believes it is appropriate to use the cancer potency (Q_1^*) from 4-chloroaniline to gauge any potential risk from 3-chloroaniline. Based on the structure of the compounds, the Agency believes that 3-chloroaniline is probably, at most, equally as potent and not likely to be more potent than 4-chloroaniline.

Two risk scenarios were used in the dietary cancer risk assessment. One scenario would be more typical of the nationwide risk to chlorpropham as this chemical is currently used. This scenario assumes that the average public is exposed to 3-chloroaniline solely through residues on stored potatoes.

The second scenario, termed the "local milkshed" scenario, describes what could be a higher exposure in rural communities where cattle are fed potato peelings. This scenario assumes that residues of 3-chloroaniline would be present in beef liver based on a cattle diet of 75% treated potato waste and in milk at half the limit of detection. It further assumes that these food commodities are distributed locally.

The cancer risk assessment from the typical nationwide scenario resulted in a risk estimate of 3×10^{-6}. The resulting risk estimate from the local milkshed assessment was 4×10^{-6}. Both of these risk estimates exceed the 1×10^{-6} estimate of individual excess lifetime cancer risk generally considered to be negligible. However, for the reasons noted below, the Agency believes these numbers likely represent an overestimation of risk. (If new chlorpropham food uses are registered in the future which would increase the dietary exposure to 3-chloroaniline, the Agency may require additional data regarding the toxicity of 3-chloroaniline.)

- Based on a study by Amdur *et al* (1991), 3-chloroaniline would not be expected to be more potent than 4-chloroaniline.
- Rat metabolism studies detected 3-chloroaniline but no 4-chloroaniline.
- An oncogenicity study of chlorpropham in rats did produce an increase in testicular Leydig cell adenomas. These benign tumors were only observed at one excessive dose level (higher than the maximum tolerated dose). Yet none of the tumor types which have been observed in 4-chloroaniline data were present in the chlorpropham studies (i.e, the 3-chloroaniline that was present in the test was not observed having a similar mode-of-action effect).

The cancer dietary risk from spinach is likely to be small compared to potatoes because of its lower consumption and lower residues. However, if the spinach use is maintained, plant metabolism and possibly field residue studies analyzing for 3-chloroaniline may be required.

MOEs were calculated for occupational handlers in high exposure potential scenarios. The resulting MOEs are all greater than 100, indicating only minimal concerns.

Environmental Assessment

All data requirements for the indoor use of chlorpropham have been fulfilled. It was not necessary to perform a risk assessment for ecological effects for the indoor use of chlorpropham.

The three outdoor uses of chlorpropham (spinach, Easter lilies, and ginkgo trees) were registered as Special Local Needs under FIFRA Section 24(c) and are not being supported by the primary registrants of technical chlorpropham. In order to maintain these registrations, environmental fate and ecological effects data will have to be submitted.

Additional Data Required

EPA is requiring additional generic residue data to confirm its regulatory assessments and conclusions for the use of chlorpropham on potatoes. The Agency is requiring additional studies in the areas of residue chemistry, ecological effects, and environmental fate to maintain the outdoor uses of chlorpropham.

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 chlorpropham end-use products must comply with EPA's current pesticide product labeling requirements. For a comprehensive list of labeling requirements, please see the chlorpropham RED document.

Minimum personal protective equipment (PPE) for all occupational handlers is chemical resistant gloves. A restricted-entry interval of 12 hours has been established for the two uses (Easter lilies and spinach) which are within the scope of the Worker Protection Standard (WPS). PPE required for persons who must enter areas that remain under a restricted-entry interval includes coveralls, chemical-resistant gloves, shoes, and socks. The Agency is requiring a respirator as PPE during application and ventilation of stored potatoes when chlorpropham is applied as an aerosol or through forced-air distribution.

The Agency is also establishing the following entry restriction for uses of chlorpropham on stored potatoes when it has been applied as an aerosol or through forced-air distribution:

> "Do not enter or allow any person, other than a person equipped with the appropriate handler personal protective equipment including a

respirator, to enter the treated area until the area has been ventilated for either a total of two (2) hours with fans or other mechanical ventilation or four (4) hours with windows, vents, or other passive ventilation or until such time as 10 complete air exchanges have occurred. The ventilation time may be interrupted, i.e., the time may be accumulated at sporadic intervals, such as 15 minutes of ventilation followed by a period with no ventilation, until the total required ventilation time has accumulated."

Chlorpropham products which are labeled for application to potatoes on a conveyor belt must contain the following statement:

"Following application, workers (e.g. baggers) must wear chemical-resistant gloves while potatoes are wet."

Regulatory Conclusion

The Agency has determined that the nationwide use of chlorpropham on stored potatoes to inhibit sprouting as currently registered will not cause unreasonable risk to humans or the environment and this use is eligible for reregistration. These products will be reregistered once the required confirmatory generic data, product specific data, CSFs, and revised labeling are received and accepted by EPA.

However, there are four registrations of chlorpropham on potatoes first registered under Section 24(c) of FIFRA in the states of North Dakota, Oregon, and Washington which have application rates not supported by field residue data. These products are eligible for reregistration, *provided* registrants of these products reduce their label application rates or submit additional field residue data to the Agency which support these higher rates.

In addition, there are currently seven chlorpropham registrations first registered under Section 24(c) of FIFRA restricted to particular states or counties for use on spinach, Easter lilies, and ginkgo trees. There are insufficient data to make a reregistration eligibility decision on these outdoor uses of chlorpropham. The Agency is requiring additional studies in the areas of residue chemistry, ecological effects, and environmental fate to maintain these uses. There are sufficient data available to support the existing interim tolerance on spinach while new data are generated.

For More Information

EPA is requesting public comments on the Reregistration Eligibility Decision (RED) document for chlorpropham 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 chlorpropham 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 chlorpropham RED, or reregistration of individual products containing chlorpropham, 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 9:30 am and 7:30 pm Eastern Standard Time, Monday through Friday.