United States Environmental Protection Agency | Prevention, Pesticides And Toxic Substances (7508C) | EPA 738-F-04-010 September 2004

R.E.D. FACTS

Carboxin

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. To implement provisions of the Food Quality Protection Act of 1996, EPA considers the special sensitivity of infants and children to pesticides, as well as aggregate exposure of the public to pesticide residues from all sources, and the cumulative effects of pesticides and other compounds with common mechanisms of toxicity. The Agency develops any mitigation measures or regulatory controls needed to effectively reduce each pesticide's risks. EPA then reregisters pesticides that meet the safety standard of the FQPA and 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 0012, carboxin.

Use Profile

Carboxin is a systemic fungicide used to control seed and seedling diseases (smut, rot, blight) on barley, beans, canola, corn, cotton, oats, onions, peanuts, rice, rye, safflower, sorghum, soybeans, triticale, and wheat. Formulations include wettable powder, dust, flowable concentrate, emulsifiable concentrate, and ready-to-use liquid. Carboxin is applied to seeds prior to planting both by commercial seed treaters and on-farm applicators. Approximately 200,000 lbs of carboxin are used annually throughout the U.S.; 140,000 for commercial use, and 60,000 for on-farm use. There are no registered residential uses for carboxin.

Regulatory History

Carboxin was first registered as a pesticide in the U.S. in 1968. EPA issued a Registration Standard for carboxin in August, 1981 (PB82-132994). Carboxin Product and Residue Chemistry Reregistration Standards updates were issued in October, 1991. Data Call-In (DCI) Notices for carboxin were issued by the Agency in 1991, 1995 and 1997. The tolerance reassessment decision for carboxin was completed in December 2002.

Human Health Assessment

Toxicity

Carboxin has been shown to have low acute toxicity. Toxicity Categories, which range from I (most toxic) to IV (least toxic), were III for the oral route of exposure, IV for inhalation, and III for dermal. Carboxin is a slight eye irritant (Toxicity Category III), is not a skin irritant (Toxicity Category IV), and is negative for dermal sensitization. The mechanism of toxicity for carboxin has not been fully investigated; however the primary target organs appear to be the liver and kidney. In carcinogenicity studies in rats and mice, carboxin did not demonstrate any significant evidence of carcinogenic potential.

Dietary Exposure

The Agency has assessed the dietary risk posed by carboxin and determined that exposure to carboxin from food and water are well below the Agency's level of concern for all populations

The chronic dietary exposure estimates for carboxin are below the Agency's level of concern (<100% cPAD) for the U.S. Population and all population subgroups: All supported commodities were less than 36% cPAD. An acute dietary risk assessment was not required since no acute dietary toxicity end-point of concern was identified. Tolerances for residues of carboxin in/on food and feed commodities are currently established under 40 CFR § 180.301. Tolerances have been reassessed for barley, bean, canola, cattle, corn, cottonseed, egg, goat, hog, horse, milk, oat, onion, peanut, poultry, rice, safflower, sheep, sorghum, soybean, and wheat products, and are detailed in the RED.

The residues of concern in drinking water are carboxin and its sulfoxide degradate. Since no monitoring data were available to assess residues of carboxin and carboxin sulfoxide in drinking water, the Agency used the FIRST and SCI-GROW models to determine surface water and groundwater estimated environmental concentrations (EECs). The surface water EEC (0.63 ppb) and groundwater EEC (0.095 ppb) were less than the DWLOC (26) indicating that chronic exposure to carboxin in food and drinking water from surface water or groundwater sources are below the Agency's level of concern.

Occupational and Residential Exposure

The results of the worker exposure assessment indicate that workers are unlikely to encounter unacceptable occupational exposure to carboxin. There are no registered residential uses for carboxin and therefore no potential for residential exposure from pesticidal uses of carboxin.

Workers may be exposed to carboxin via dermal and inhalation routes during loading, treating, and planting activities. Seven major exposure scenarios were identified as representative of carboxin uses: (1) on farm seed treatment with dry

formulations - open transfer system, (2) on farm seed treatment with liquid formulations - closed transfer system, (3) loading and applying liquid with commercial seed-treatment equipment, (4) bagging and otherwise handling treated seeds with commercial equipment, (5) commercial sewer stitching bags of seed, (6) multiple commercial seed treatment activities and (7) loading and planting treated seeds.

Worker risk is measured by a Margin of Exposure (MOE) which determines how close the occupational exposure comes to the No Observable Adverse Effect Level (NOAEL) taken from an animal study. A MOE of 100 or greater for both the dermal and inhalation route is considered to be adequately protective for carboxin. The results of the worker exposure assessment indicate that all potential exposure scenarios result in MOEs greater than or equal to the target MOE of 100 at the baseline level of protection for all routes of exposure (i.e., dermal, inhalation, and aggregate dermal and inhalation).

FQPA Considerations

No Special FQPA Safety Factor is necessary to protect the safety of infants and children because there is no quantitative or qualitative evidence of increased susceptibility following in utero or postnatal exposure in any of the developmental or reproductive studies, and the toxicity endpoints selected are protective of pre/postnatal toxicity following acute and chronic exposures.

Carboxin is classified as "not likely to be carcinogenic to humans " according to the EPA *Draft Proposed Guidelines for Carcinogen Risk Assessment* (July 2, 1999).

Environmental Assessment

Environmental Fate

Carboxin is a very mobile compound that degrades rapidly in soil by aerobic metabolism with a mean half-life of 1.25 days. Carboxin degraded much more slowly in anaerobic soil with a half-life of 128 days. In both aerobic and anaerobic soil studies, the predominant degradate was carboxin sulfoxide which forms quickly, is more persistent, and is more mobile than the parent compound. Based on the structure of carboxin sulfoxide, the toxicity of the sulfoxide degradate is likely comparable to that of the parent compound carboxin.

There was no evidence of degradation by hydrolysis at any pH for carboxin. Aqueous photolysis is rapid with a half-life of 1.5 hours under a xenon arc lamp. Photolysis is not expected to be a major route of dissipation in the field as planted seed is generally buried some depth below the surface, but may contribute to dissipation after it has entered surface water bodies. Degradation in the anaerobic phase in soil was much slower with a mean degradation half-life of 129 days. There is some evidence that carboxin may degrade by direct oxidation in aqueous systems when dissolved oxygen is present. Limited information on aquatic

metabolism show slower degradation rates anaerobically (245 days) than aerobically (31 days). In two anaerobic soil metabolism studies conducted for carboxin sulfoxide, the major degradate formed was carboxin, indicating that carboxin can reform from the sulfoxide under anaerobic conditions.

Ecological Effects

Mammals and birds in the field may be exposed to carboxin by ingesting treated seeds or by other routes, such as incidental ingestion of contaminated soil, dermal contact with treated seed surfaces and soil during activities in the treated areas, inhalation of pesticide vapor and contaminated particulate, and ingestion of drinking water contaminated with the pesticide.

Based on the ecological effect studies, carboxin is practically nontoxic to terrestrial animals and ranges from moderately to slightly toxic to aquatic animals on an acute exposure basis. No data were available to gauge the acute toxicity of carboxin to estuarine/marine fish. Following chronic exposure, mallard ducks (Anas platyrhynchos) exhibited reductions in the number of eggs laid, viable embryos, live 3-week embryos, normal hatchlings and 14-day survivors at 700 mg/kg/day. Chronic exposure to rats (Rattus norvegicus) resulted in reduced growth (decreased body weight) of offspring. Based on environmental concentrations in surface water, no acute LOCs are exceeded for aquatic animals or plants. No chronic toxicity data were available for the Agency to review and based on the use pattern, no chronic exposure for aquatic animals and plants is expected.

The Agency has developed the Endangered Species Protection Program to identify pesticides whose use may cause adverse impacts on endangered and threatened species, and to implement mitigation measures that address these impacts. Thus far, the only endangered seed-eating animal that requires risk mitigation is the Attwater's Prairie Chicken (*Tympanuchus cupido attwateri*).

EPA will continue to evaluate whether currently identified and/or additional endangered species may be impacted by exposure to carboxin and is working with other federal, state, and local agencies to refine the endangered species risk assessment with the goal of developing reasonable and prudent alternatives to mitigate risks to endangered species.

Risk Mitigation

The Agency has determined that the current risk mitigation strategies for carboxin are acceptable. Carboxin is a very mobile compound that degrades rapidly in soil, and is not registered for aquatic application. There are no registered residential uses for carboxin and therefore no potential for residential exposure from pesticidal uses of carboxin. All potential occupational exposure scenarios result in MOEs greater than or equal to the target MOE of 100 at the baseline level of protection for all routes of exposure (i.e., dermal, inhalation, and aggregate dermal

and inhalation). Mammals and birds in the field may be exposed to carboxin by ingesting treated seeds or by other routes, but the predicted exposure from these routes are below the Agency's LOCs.

The Agency's initial assessment suggested that eight endangered species may potentially be impacted by carboxin: the Delmarva fox squirrel (*Sciurus niger cinereus*), six species of kangaroo rat *(Dipodomys spp*.), and the Attwater's Prairie Chicken (*Tympanuchus cupido attwateri*). Based on information provided by the U.S. Fish and Wildlife Service, the endangered species profile, and communications with refuge managers, risk mitigation is required only for the Attwater's Prairie Chicken (*Tympanuchus cupido attwateri*). The Agency will issue new or revised County Specific Bulletins for the Attwater's Prairie Chicken to be issued in Austin, Colorado, and Galveston Counties in Texas. The bulletins will require minimum planting depths (rice 0.5 inch, cotton 1.5 inch) and subsequent discing for carboxin-treated seed planted within one mile of the U.S. Fish and Wildlife Service's Attwater Prairie Chicken National Wildlife Refuge and The Nature Conservancy's Texas City Preserve.

In conjunction with other local and federal agencies, EPA will continue to evaluate whether currently identified and/or additional endangered species may be impacted by exposure to carboxin.

Additional Data Required

EPA requires additional generic studies for carboxin to confirm its regulatory assessments and conclusions.

Most data requirements are satisfied for the 97% carboxin T/TGAI; however, additional data are required:

830.1620	Description of Production Process
830.7050	UV/Visible Absorption
835.1230	Sediment and Soil Adsorption/Desorption for Parent and Degradates
835.1240	Soil Column Leaching
835.2410	Photodegradation of Parent and Degradates in Soil
850.1035	Acute Toxicity Test for Estuarine and Marine Organisms
850.1400	Fish Early-Life Stage Toxicity Test
850.1300	Daphnid Chronic Toxicity Test
860.1340	Residue Analytical Method

860.1500	Crop Field Trials
870.3465	28-Day Inhalation Toxicity

Additional product chemistry data are required for the carboxin 75% formulation intermediate (FI).

The Agency is uncertain regarding the endocrine disrupting potential of carboxin and, once the appropriate testing protocols have been established for examining endocrine disruption, carboxin may be subject to this battery of tests.

Product Labeling Changes Required

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

Regulatory Conclusion

The use of currently registered products containing carboxin 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.

Carboxin 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 carboxin 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 Information and Records Integrity Branch, Information Resources and Services Division (7502C), Office of Pesticide Programs (OPP), US EPA, Washington, DC 20460, telephone 703-305-5805.

Electronic copies of the RED and this fact sheet are available on the Internet. See http://www.epa.gov/REDs.

Printed copies of the RED and fact sheet can be obtained from EPA's National Service Center for Environmental Publications (EPA/NSCEP), PO Box 42419, Cincinnati, OH 45242-2419, telephone 1-800-490-9198; fax 513-489-8695.

Following the comment period, the carboxin RED document also will be available from the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22161, telephone 1-800-553-6847, or 703-605-6000.

For more information about EPA's pesticide reregistration program, the carboxin RED, or reregistration of individual products containing carboxin, please contact the Special Review and Reregistration Division (7508C), 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 Pesticide Information Center (NPIC). Call toll-free 1-800-858-7378, from 6:30 am to 4:30 pm Pacific Time, or 9:30 am to 7:30 pm Eastern Standard Time, seven days a week. Their internet address is http://npic.orst.edu.