United States Environmental Protection Agency | Prevention, Pesticides And Toxic Substances (7508C) | EPA-738-F-99-008 APRIL 1999

R.E.D. FACTS

CHLOROTHALONIL

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 0097, chlorothalonil, or 2,4,5,6-tetrachloroisophthalonitrile.

Use Profile

Chlorothalonil acts primarily as a fungicide and mildewicide, but also has some activity as a bactericide, microbiocide, algaecide, insecticide, and acaricide. It is a broad spectrum, non-systemic pesticide. Its exact mechanism of action is not known. Chlorothalonil is registered on a wide variety of sites including field, vegetable, and orchard crops; turf; and as a mildewicide to be added to paint and other surface treatments. There are currently 39 tolerances for chlorothalonil. Application methods include hand-held duster or granule spreader; backpack sprayer; chemigation; ultra-low, low, or high volume ground sprayer; aircraft; air-blast; specialty air-assisted equipment; brush-on and dip treatments; airless sprayers; and thermal fog generator. Chlorothalonil is formulated in dust, granular (dry and water dispersible), wettable powder, dry flowable, flowable concentrate, impregnated material, or ready-to-use

formulations. Homeowner uses include mildewicidal additive for paint, ornamental plants, and turf uses.

Regulatory History

Chlorothalonil was first registered in the United States in 1966 for use on turfgrass. GB Biosciences, Veterans Ilex, Sipcam Corporation, Thor Chemie GMBH, and Westbridge Industries all hold registrations for manufacturing-use product, but of these registrants, only the first two manufacture technical grade active ingredient. A Registration Standard was issued by the Agency for chlorothalonil in September 1984. There are 101 chlorothalonil products registered, along with 98 Special Local Needs registrations (SLNs). Chlorothalonil is not a restricted use pesticide.

Human Health Assessment

Toxicity

Chlorothalonil is in acute Toxicity Category IV (the least toxic of four categories) for the oral route of exposure, and in Toxicity Category II for the inhalation route. For acute dermal effects and acute skin irritation, chlorothalonil is in Toxicity Category IV. Chlorothalonil produces severe eye irritation in rabbits (Toxicity Category I). The Agency has classified chlorothalonil as a likely human carcinogen (formerly Group B2).

In determining whether to retain, reduce, or remove the 10x FQPA safety factor for infants and children, EPA uses a weight of evidence approach taking into account the completeness and adequacy of the toxicity data base, the nature and severity of the effects observed in pre- and post-natal studies, and exposure. The developmental and reproductive data for chlorothalonil indicate that there is no evidence of an increased sensitivity to chlorothalonil from pre- or post-natal exposures. In a rat study, the developmental LOEL was based on resorptions and post-implantation loss. The same dose was associated with maternal effects. No developmental toxicity was observed at any dose level in a rabbit study, and no maternal toxicity was observed at the highest dose tested (20 mg/kg/day). No reproductive effects were observed in any study, and developmental effects occurred only in the presence of significant maternal toxicity.

Based on these findings, the Agency has concluded that the ten-fold safety factor applied according to FQPA to account for special sensitivity to infants and children is not warranted for chlorothalonil, and should be removed.

SDS-3701 is the major metabolite of chlorothalonil. In acute toxicity testing, it is placed in Toxicity Category II for the oral route of exposure. There is no evidence of carcinogenicity for the SDS-3701 metabolite.

Hexachlorobenzene (HCB) is an impurity present in chlorothalonil and other pesticide products. It is classified as a B2 carcinogen.

Dietary Exposure and Risk

Chlorothalonil in Food: To estimate acute dietary risk from food, exposure estimates for chlorothalonil and the metabolite SDS-3701were compared to a LOEL of 175 mg/kg/day, based on cell proliferative response in rats. Because a LOEL was used for the assessment instead of a NOEL, an extra safety factor of 3 was added, and the safety margin is 300 instead of 100. The acute dietary risk analysis for chlorothalonil and SDS-3701 combined indicates that there are adequate margins of exposure for the general population and the most highly exposed population subgroups.

To estimate chronic non-cancer dietary risk from food, dietary exposure estimates for chlorothalonil and SDS-3701 were compared to the RfD for chlorothalonil, 0.02 mg/kg/day, derived from a 2-year feeding study in rats which exhibited kidney and stomach effects. An uncertainty factor of 100 was applied to account for intraspecies variability and interspecies extrapolation. Dietary exposure was estimated from tolerance level residues adjusted with information on how much of each crop is actually treated with chlorothalonil. Risk estimates indicate that chronic non-cancer dietary risk from exposure to chlorothalonil and SDS-3701 combined is not of concern for the general population and the most highly exposed population subgroup.

Chlorothalonil dietary cancer risk estimates are calculated from both the Q_1^* for chlorothalonil (0.00766 $[mg/kg/day]^{-1}$, based on tumor rates in female rats), resulting in a measure of cancer probability, and the NOEL (1.5 mg/kg/day, derived from a cell proliferation study in mice), resulting in a margin-of-exposure measure of risk. Risk management decisions were based on the Q_1^* formula, as the non-linear mechanism associated with the MOE approach has not been definitively validated and policy on determining an adequately protective MOE for cancer risk has not been established. Cancer

risk from food was estimated to be 1.2×10^{-6}. This figure is at a level which the Agency considers negligible for excess lifetime cancer risk estimates.

Chlorothalonil in water: In estimating acute and chronic non-cancer drinking water risks from groundwater, concentrations of chlorothalonil were estimated as the combined concentrations of its metabolites as found in an area of vulnerability to groundwater contamination. Chlorothalonil itself was not found in this area, and found infrequently in groundwater from other areas. Because chlorothalonil was not generally found in groundwater, and because the metabolites which were found are not known to be carcinogenic, cancer risk for drinking water from groundwater sources was not assessed.

For acute risk from groundwater sources of drinking water, the highest combined metabolite concentration in groundwater was compared to the acute dietary exposure LOEL of 175 mg/kg/day. This acute risk drinking water assessment for groundwater indicated that there are adequate margins of exposure for the general population and the most highly exposed population subgroups.

For chronic non-cancer risk from groundwater sources of drinking water, the highest combined metabolite concentration in groundwater was compared to the compared to the RfD of 0.02 mg/kg/day. This assessment indicates that chronic non-cancer drinking water risk from groundwater is not of concern for the general population and the most highly exposed population subgroup.

Chlorothalonil has been detected in surface water, and acute, chronic non-cancer, and cancer drinking water risks were based on the maximum concentration detected in surface water monitoring in southern Florida.

For acute risk from surface water sources of drinking water, the maximum detected concentration in surface water was compared to the acute dietary exposure LOEL of 175 mg/kg/day. This acute risk drinking water assessment for surface water indicates that there are adequate margins of exposure for the general population and the most highly exposed population subgroup.

For chronic non-cancer risk from surface water sources of drinking water, the maximum detected concentration in surface water was compared to the compared to the RfD of 0.02 mg/kg/day. This assessment indicates that chronic non-cancer drinking water risk from groundwater is not of concern for the general population and the most highly exposed population subgroup.

Chlorothalonil dietary cancer risk estimates were based on both the Q_1^* for chlorothalonil and the NOEL from the cell proliferation study. As noted above, risk management decisions were based on the Q_1* formula. Using the Q_1*, drinking water cancer risk from surface water is estimated to be well below the level which the Agency considers negligible for excess life time cancer risk estimates.

SDS-3701: The acute and chronic non-cancer dietary risk assessments for SDS-3701 in food are folded into the assessments for chlorothalonil. Acute and chronic non-cancer dietary risks for SDS-3701 in groundwater are addressed through the use of a maximum combined metabolite concentration as a surrogate exposure for chlorothalonil concentrations. Surface water drinking water risks were not estimated for SDS-3701 due to a lack of data. SDS-3701 is not carcinogenic, so dietary cancer risks for food and drinking water were not assessed.

HCB from chlorothalonil in food: There is no acute endpoint associated with HCB, so acute dietary risks were not assessed. Chronic non-cancer dietary risk from food was estimated by comparing the RfD for HCB (0.0008 mg/kg/day, based on liver effects in a 130-week rat feeding study) to dietary exposure. In the absence of HCB monitoring data, dietary exposure was estimated from tolerance level residues of chlorothalonil adjusted with information on how much of each crop is actually treated with chlorothalonil and further adjusted for a maximum level of 0.05% HCB in the formulation. Risk estimates for the overall U.S. population and the most highly exposed subgroup indicate that chronic non-cancer dietary risk from exposure to HCB in chlorothalonil is not of concern for the general population and the most highly exposed population subgroup.

Dietary cancer risk from food for HCB in chlorothalonil was based on the Q_1* for HCB and the dietary exposure estimate described above. The Q_1*

for HCB, 1.02 $(mg/kg/day)^{-1}$, is based on tumor incidence in hamsters and rats. The dietary cancer risk estimate from food for HCB in chlorothalonil is below the level which the Agency considers negligible for excess life time cancer risk estimates.

HCB from chlorothalonil in drinking water: Estimates of the drinking water risk for HCB originating in chlorothalonil were not calculated for acute risk because HCB has no acute risk endpoint. Chronic non-cancer drinking water risk for HCB from chlorothalonil in groundwater was estimated by assuming HCB is present in drinking water at 0.05% of the maximum combined metabolite concentration. The estimated exposures were compared to the RfD of 0.0008 mg/kg/day. This assessment indicates that chronic non-cancer drinking water risk from groundwater for HCB originating in chlorothalonil is not of concern for the general population and the most highly exposed population subgroup. Drinking water cancer risk for HCB from chlorothalonil in groundwater was not calculated because the metabolites represented by the maximum combined metabolite concentration in groundwater are not known to be carcinogenic.

Chronic non-cancer drinking water risks for HCB from chlorothalonil in surface water were estimated by assuming HCB is present in drinking water at 0.05% of the maximum concentration observed in surface water. The estimated exposures were compared to the RfD of 0.0008 mg/kg/day. This assessment indicates that chronic non-cancer drinking water risk from surface water for HCB originating in chlorothalonil is not of concern for the general population and the most highly exposed population subgroup.

For estimating drinking water cancer risk for HCB originating in chlorothalonil from surface water, the estimated concentration of HCB (0.05% of the maximum chlorothalonil concentration observed in surface water) was compared to the cancer potency factor for HCB, 1.02 $(mg/kg/day)^{-1}$. The estimated drinking water cancer risk for HCB originating in chlorothalonil from surface water is well below the level considered by the Agency to be negligible for excess lifetime risk.

HCB from all pesticidal sources in the diet: HCB is present in chlorothalonil and at least nine other pesticides. Four of these contribute

significant amounts of HCB and pentachlorobenzene (a related contaminant that is assumed to be toxicologically equivalent to HCB) to the diet: chlorothalonil, PCNB, picloram, and dacthal. The Agency assessed the aggregate dietary cancer risks (from food and water) associated with these pesticides. The assessment is limited in particular by the lack of data on HCB levels in food and water. Food exposures were generally estimated by applying maximum contamination levels of HCB in product formulations to observed levels of parent compound residues in food. Aggregate dietary cancer risk for HCB and PCB in food was based on these exposure estimates and on the Q_1^* for HCB. The estimated dietary cancer risk for food from HCB in pesticides is 1.8×10^{-6}, which is at the lower end of range of concern for dietary cancer risk.

A quantitative aggregate assessment for HCB and PCB in drinking water was not conducted because data are limited and observed levels are very low. The Agency concluded that drinking water risk estimates from HCB in pesticides did not exceed the Agency's level of concern

Occupational and Residential Exposure and Risk

Handlers: Occupational and residential risks were estimated for mixers, loaders, applicators, and flaggers (occupational only) of chlorothalonil for short- and intermediate term inhalation and dermal exposures. A dermal NOEL of 600 mg/kg/day was selected for assessing these risks from a 21-day study in the rat. The inhalation NOEL of 2 mg/kg/day was selected from a 2-year feeding study in rats. Carcinogenic risks were also assessed for handlers, based on the Q_1^*. The MOE approach was not used to estimate cancer risk for handlers because exposures to handlers were judged not to chronic.

Occupational and residential handler short- and intermediate term risk estimates were below an MOE of 100 for:

- wettable powder formulations (inhalation exposure),
- granulars applied with tractor drawn spreaders to turf (inhalation exposure),
- specialty air-assisted equipment on golf courses (dermal exposure),
- residential applicators using certain equipment on turf (dermal and some inhalation exposure), and
- professional painters using sprayers (inhalation exposures).

Occupational and residential cancer risk estimates (using the Q_1*) exceeded levels which typically are of concern for:

- wettable powder formulations, and
- residential applicators using certain equipment on turf.

Handler risks from exposure to HCB in chlorothalonil were approximated using a high-end exposure estimate for chlorothalonil and adjusted for the maximum allowable concentration of HCB in chlorothalonil. By this approach, handler risks from HCB were determined to be below the levels the Agency typcially identifies as being of concern.

Post-Application: The Agency has assessed the interim restricted entry interval (REI) for chlorothalonil of 48 hours. The Agency now believes that a 12-hour REI is appropriate if additional measures are taken to protect the eyes for seven days after chlorothalonil is applied.

Significant post-application exposures were thought to be possible in a number of settings including workers who maintain and harvest horticultural crops and residents exposed to treated lawns. Short- and intermediate-term post-application risks for chlorothalonil were based on the same dermal NOEL as handler risks. Post-application inhalation exposures were determined not be significant. Carcinogenic risk was estimated using the Q_1* approach. Exposures to workers who reenter treated areas to perform hand-labor tasks on cut flowers may be chronic, so cancer risk for these workers also was calculated using the MOE approach.

Short- and intermediate-term post-application risks were below the MOE of 100 for two scenarios:

- workers reentering treated sodfarm areas to cut, roll, and harvest sod
- toddlers in dermal contact with treated turf.

None of post-application cancer risk estimates based on the Q_1* showed excess cancer risk. For workers reentering treated greenhouses and fields where flowers and potted ornamentals are grown for hand-labor tasks (cutting, bundling, transplanting, and pruning), cancer risk estimates based on the MOE

approach are likely to exceed the standards which will be established by the Agency for acceptable cancer MOEs. This assessment is predicated on the potential for chronic exposures to workers in these areas, an assumption which the Agency is requiring data to confirm. Although the Agency has not confirmed that the non-linear mechanism on which the cancer MOE approach is based is valid, and has not identified an "acceptable" MOE for cancer, past discussions of an acceptable level have focused on MOEs of 100 or greater. An MOE of less than 100, as has been calculated for these workers, is likely to be of concern.

Environmental Assessment

Environmental Fate

Chlorothalonil is resistant to hydrolysis, photolysis, and volatilization, and only moderately susceptible to degradation in soil under aerobic conditions. Chlorothalonil is somewhat persistent in water when microbial activity is limited and hydrological residence times are long. Aerobic aquatic metabolism half-lives from two hours to eight days have been reported under various conditions, but the two-hour half-life is associated with experimental conditions which correspond more closely to aerated and agitated wastewater treatment than to natural systems. Even so, the shorter half-life was used as a low-end assessment parameter in the RED.

Chlorothalonil has limited potential to reach groundwater, and where it has been detected in groundwater, concentrations have been low and often attributed to atypical sources. Degradates of chlorothalonil have been found in groundwater. Chlorothalonil can contaminate surface water via spray drift or through runoff and erosion. Chlorothalonil can be dissolved in runoff and adsorbed to sediment in the runoff.

The major degradate of chlorothalonil in the soil under aerobic conditions is SDS-3701. SDS-3701 appears to be more persistent and mobile than chlorothalonil. Consequently, substantial amounts of SDS-3701 may be available for runoff for longer periods than chlorothalonil and SDS-3701 may be more persistent in water/sediment systems than chlorothalonil.

The bioaccumulation potential of chlorothalonil is low, although there is some potential for the bioaccumulation of chlorothalonil degradates in oysters.

Ecological Effects

Chlorothalonil is "practically non-toxic" to avian species on an acute oral and subacute dietary basis, and effects on avian reproduction have been observed at a dose of 5 ppb. Chlorothalonil is "practically non-toxic" to small mammals on an acute oral basis, and developmental effects were observed in rats at 8 ppb. Chlorothalonil is "relatively non-toxic" to honey bees, and "very highly toxic" to fish. The toxicity of formulated chlorothalonil products to fish is similar but may be affected by other constituents in the products. Fathead minnow hatching success and survival are affected at concentrations of chlorothalonil between 3 and 6.5 ppb. Chlorothalonil is "very highly toxic" or "highly toxic" to aquatic invertebrates, and a formulated chlorothalonil product showed similar results. Chlorothalonil can affect aquatic invertebrate reproduction between 39 and 79 ppb.

SDS-3701 is more toxic to birds than the parent on an acute oral and subacute dietary basis; avian reproduction in birds could be affected at levels above 50 ppm. SDS-3701 is "moderately toxic" to small mammals on an acute oral basis. SDS-3701 is "slightly toxic" to bluegill and *D. magna*, and significantly less toxic than parent chlorothalonil in both cases.

At an application rate of 16 lb chlorothalonil/A, the most sensitive terrestrial plant species (onions) showed a non-statistically significant negative response in seed germination/seedling emergence/vegetative vigor. Testing in a freshwater green alga exhibited an EC_{50} of 190 ppb and a NOEC of 50 ppb. Additional Tier 2 testing for aquatic species is required.

Ecological Effects Risk Assessment

Levels of concern, especially for aquatic organisms, were exceeded for a number of crops, including peanuts and potatoes. The turf use can also be high risk. In addition, many chlorothalonil labels do not provide specific application rate maximums. Marine/estuarine mollusks are particularly at risk.

Risk Mitigation

To address the carcinogenic dietary risk from HCB contributed by chlorothalonil, the registrants of chlorothalonil have agreed to reduce the level of HCB in chlorothalonil technical and manufacturing-use products to 40 ppm by January 1, 2003. This is the lowest level that has been shown to be technologically feasible for chlorothalonil. The registrants have agreed to

certify this final level and several interim levels. Failure to achieve any milestone will result in a suspension of manufacture or import of the subject products until such time as the target level is achieved. If the target level is not achieved by January 1, 2008, the subject registrations will be immediately canceled without opportunity for appeal. The registrants have also agreed to maintain approximately historic levels of production and import of chlorothalonil manufacturing-use product during the period of HCB reduction to assure that chlorothalonil with higher concentrations of HCB will not be stockpiled and formulated. The schedule for interim reductions in HCB content is different for product destined to be added to paint and all other products in recognition of pigmentation problems which may be associated with purification, but the final date and contamination level are the same for both.

To protect occupational handlers of pesticides containing chlorothalonil, the registrants have agreed that:

- wettable powder formulations must be packaged in water soluble bags or labeled for use only in closed mixing/loading systems,
- handlers of granular formulations applied with tractor drawn spreaders to turf must wear dust masks,
- applicators using specialty air-assisted application equipment on turf must wear chemical-resistant gloves,
- painters using airless sprayers should wear respirators,
- workers who reenter treated areas after the restricted-entry interval but within 7 days of treatment must receive special notification about eye irritation hazards and have access to on-site eye-flushing equipment,
- handlers of wettable powder, liquid flowable, and dry flowable formulations, and those using hand-held equipment (such as backpack sprayers) must wear gloves, and
- handlers in enclosed spaces (greenhouses) must wear respirators.

To protect residential handlers of pesticides containing chlorothalonil and children who are exposed to chlorothalonil after application of chlorothalonil to home lawns, the registrants have agreed that products containing chlorothalonil are prohibited for use on home lawns.

To protect reentry workers who cut, roll, and harvest sod treated with chlorothalonil, the registrants have agreed that sod treated with chlorothalonil must be harvested, rolled, and palletized mechanically.

To address risk concerns and uncertainties about exposure from specialty products, the registrants agreed that:

- chlorothalonil mildewicidal additives must be labeled to prohibit sale over-the-counter at retail outlets. The registrants have committed to working with the Agency to develop measures for the protection of employees of paint sales outlets who mix mildewicidal additives into paint for sale.
- the in-container preservative use of chlorothalonil will be discontinued.

Additionally, to address risk concerns associated with a smoke generator formulation, such products are designated as Restricted Use Pesticides, and restrictions and labeling requirements designed to reduce handler and post-application exposure are specified.

To protect wildlife, the registrants have agreed to reduce individual and seasonal maximum application rates for many use sites. For a table of these rates, refer to Chapter IV of the chlorothalonil RED. In addition, untreated buffers are required between estuarine/marine water bodies and agricultural crops treated with chlorothalonil–at least 150 feet for aerial and air-blast applications and 25 feet for ground applications.

Additional Data Required

The generic data base supporting the reregistration of chlorothalonil has been reviewed and determined to be substantially complete. The following additional data are being required:

72-3 (d-f)	Acute marine/estuarine fish, mollusk, and shrimp
72-4(a)	Fish early life stage
123-2	Aquatic plant growth
132-1(a)	Foliar residue dissipation
133-3	Post-application dermal passive dosimetry exposure
133-4	Post-application inhalation passive dosimetry exposure

(Guidelines 133-3 and 133-4 are reserved pending review of agricultural and residential post-application/reentry exposure data currently being developed by the Agricultural Reentry Task Force and Outdoor Residential Exposure Task Force.)

Residue data have been submitted in support of establishing a tolerance on sweet corn forage and are currently under review. The review of these data should not delay a reregistration eligibility decision for chlorothalonil, but additional storage stability information is required. This information is expected to confirm that chlorothalonil residues of concern are stable under frozen storage.

A special study is being required to assess residues of SDS-3701 on foliage which serves as a wildlife food source. Data on use patterns of chlorothalonil on cut flowers, particularly those grown in greenhouses, are required to determine whether post-application exposure should be considered chronic exposure. Exposure data for handlers involved in wood pressure treatment are required. Data are also required on exposures to occupational and residential handlers associated with the application of wood preservative products and people who are exposed to pressure-treated wood when they cut and build with it.

Product Labeling Changes Required

All chlorothalonil end-use products must comply with EPA's current pesticide product labeling requirements and with those labeling requirements imposed in the chlorothalonil RED. For a comprehensive list of labeling requirements, please see Section V. of the chlorothalonil RED document.

Regulatory Conclusion

The Agency has determined that chlorothalonil products, labeled and used as specified in the RED, will not pose unreasonable risks to humans or the environment.

For More Information

EPA is requesting public comments on the RED document for chlorothalonil 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 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 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 chlorothalonil RED document also will be available from the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22161, telephone 703-605-6000.

For more information about EPA's pesticide reregistration program, the chlorothalonil RED, or reregistration of individual products containing chlorothalonil 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 Telecommunications Network (NPTN). Call toll-free 1-800-858-7378, between 6:30 am and 4:30 pm Pacific Time, Monday through Saturday. Their internet address is: ace.orst.edu/info/nptn.