United States Environmental Protection Agency | Prevention, Pesticides And Toxic Substances (7508C) | EPA-738-F99-016 September 1999

R.E.D. FACTS

Folpet

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 0630, folpet.

Use Profile

Folpet is a fungicide used to control scab (sphaceloma) on avocados; wood rot fungi, mold/mildew, and spoilage fungi on wood and other surfaces.

Formulations include liquid, ready to use, 0.3 to 0.7%; wettable powder, 44 to 50%; and technical, solid 88%.

Folpet is applied by dip treatment, foliar treatment, soaking, spraying, and as a paint additive, wood surface treatment, and high volume spray.

Regulatory History

Folpet was first registered as a pesticide in the U.S. in 1948. EPA issued a Registration Standard for folpet in June 1987. A January 1993 Data Call-In (DCI) required additional data.

Currently, four folpet manufacturing use products are registered and twelve end-use products are registered. The registrant has requested voluntary cancellation of two end-use products, EPA registrations 66222-8 and 7401-231, which have been suspended for lack of supporting data. The cancellations are being processed. The proposed cancellation was published in the *Federal Register* on August 4, 1999 for a 180 day comment period. The RED assumes that these uses will be canceled in the near future.

Human Health Assessment

Toxicity

In studies using laboratory animals, folpet generally has been shown to be of low acute toxicity. However, it is moderately toxic by the inhalation route and has been placed in Toxicity Category II (the second highest of four categories) for this effect. Folpet has also been placed in Toxicity Category II for eye irritation.

Dietary Exposure

People may be exposed to residues of folpet through the diet. Tolerances or maximum residue limits have been established for apples, avocados, cranberries, cucumbers, grapes, lettuce, melons, onion (dry bulb), strawberries, and tomatoes (see 40 CFR 180.191). EPA has reassessed the folpet tolerances and found that tolerances for apples, cranberries, cucumbers, grapes, lettuce, melons, onion (dry bulb), strawberries, and tomatoes must be converted to import tolerances because the US registrations for these commodities are being canceled. Also, a new tolerance must be established for raisins because folpet concentrates in raisins. The avocado tolerance is being amended to indicate that it is limited to a regional registration for the state of Florida.

The Codex Alimentarius Commission has established temporary maximum residue limits (TMRL) for folpet on cucumber, grapes, potatoes, and strawberries.

EPA has assessed the dietary risk posed by folpet, considering food and water sources of potential residues, and quantifying dietary exposure on acute and chronic bases. For the acute dietary (food only) assessment, EPA used a probablistic exposure analysis, finding that the acute population adjusted dose (aPAD) was below the Agency's level of concern. A risk estimate that is less than 100% of the acute population adjusted Dose (acute PAD)—that is, the dose at which an individual could be exposed on any given day and no adverse health effects would be expected—does not exceed the Agency's risk concern. At the 99.9th percentile, exposure to the most sensitive sub-group (females age 13-50) was found to be about 25% of the aPAD for folpet.

EPA also assessed the chronic (non-cancer) dietary risk using average field trial data and percent crop treated information. The Agency found that the chronic population adjusted dose (cPAD) was below the Agency's level of concern. A risk estimate that is less than 100% of the cPAD—the dose at which an individual could be exposed and not expect an adverse health effect—does not exceed the Agency's risk concern. For all subgroups, the exposure is less than 1% of the cPAD for folpet.

In addition, EPA assessed the dietary cancer risk from residues in food using the same exposure information as used in the chronic (non-cancer) assessment and a cancer potency factor or Q_1* of 0.00186 $(mg/kg/day)^{-1}$. The Agency found a cancer risk of 9.8×10^{-8} for folpet, which is less than the Agency's level of concern of 1×10^{-6}.

The dietary risk from water, as well as the aggregate risk assessment for folpet is discussed in the FQPA Considerations portion of this factsheet.

Occupational and Residential Exposure

Based on current use patterns, handlers (mixers, loaders, and applicators) may be exposed to folpet during and after normal use of the wettable powder and liquid ready to use formulations in agricultural, residential, and manufacturing settings.

Human Risk Assessment

Folpet generally is of medium acute toxicity, but causes developmental effects in animal studies and has been classified as a Group B2, probable human carcinogen. Food crop uses are registered including avocados in the US and apples, cranberries, cucumbers, grapes, lettuce, melons, onions, strawberries, and tomatoes imported from other countries However, dietary exposure to folpet residues in foods is extremely low, as is the cancer risk posed to the general population.

Of greater concern is the risk posed to folpet handlers, particularly mixers/loaders who come into contact with folpet while adding it to paint during manufacture. Exposure and risk to workers will be mitigated by the use of PPE required by the WPS, supplemented by a dust/mist respirator and chemical resistant gloves as required by this RED. Post-application reentry workers will be required to observe a 24-hour Restricted Entry Interval, which is set by the WPS. For folpet, a 24-hour REI is required because folpet is classified as Toxicity Category II for acute inhalation toxicity and for eye irritation.

FQPA Considerations

The Agency has determined that the established tolerances for folpet, with amendments and changes as specified in this document, meet the safety standards under the FQPA amendments to section 408(b)(2)(C) of the FFDCA, and that there is a reasonable certainty of no harm for infants and children. The safety determination for infants and children considers the factors noted above for the general population, but also takes into account the possibility of increased dietary exposure due to the specific consumption patterns of infants and children, as well as the possibility of increased susceptibility to the toxic effects of folpet residues in this population subgroup.

In determining whether or not infants and children are particularly susceptible to toxic effects from folpet residues, EPA considered the completeness of the database for developmental and reproductive effects, the nature of the effects observed, and other information.

Based on the current data requirements, folpet has a complete database for developmental and reproductive toxicity. Reliable studies cited earlier in this document indicate limited concern for special sensitivity of young organisms to folpet (see Section IIIb). However, the Agency has determined that the Safety Factor can be reduced to 3X based on the developmental and reproductive toxicity studies available for folpet, as described previously in Section III(B)1(d) of this document. The Agency has retained a 3X FQPA safety factor to ensure adequate protection of infants and children. This FQPA safety factor applies only to females 13-50 for acute and short-term exposures. Therefore, the Agency has concluded that a total uncertainty factor of 300 is adequate to protect infants and children. This uncertainty factor was incorporated into the risk assessment.

At this time, the Agency does not know how to apply the information in its files concerning common mechanism issues to most risk assessments; however, there are pesticides for which the common mechanism issues can be resolved. For example, there are pesticides that are toxicologically dissimilar to existing chemical substances, in which case the Agency can conclude that it is unlikely that a pesticide shares a common mechanism of activity with other substances. There are also pesticides that produce a common toxic metabolite, in which case common mechanism of activity will be assumed.

In the case of folpet, the Agency is aware of a proposed common mechanism of carcinogenicity with captan. Captan and folpet share a common metabolite, thiophosgene, which is believed to be responsible for the carcinogenic effects observed with both compounds. Thiophosgene is a highly reactive, short-lived

species which is produced in the gut and believed to cause tumors through the irritation of the duodeum. Because it is so short lived, its residues cannot be quantified. Without measurable residues of the common metabolite, it is difficult at this time to relate exposures of captan to those of folpet since the rate of formation of thiophosgene may be different for both compounds. However, assuming that the carcinogenic effects observed in both pesticides are due solely to the metabolite thiophosgene, the Agency believes it is reasonable to add the estimated cancer risks from the individual aggregate risks from both folpet and captan to obtain a worse case estimate. When this is done, the risks do not exceed the Agency's level of concern.

The Agency considers residential postapplication exposure to folpet from its use in sealants and coatings to be negligible because dermal and inhalation exposures are likely to be minimal. Therefore, EPA has considered only residential handler exposure together with dietary and drinking water exposures in its aggregate risk assessment.

In assessing acute aggregate dietary risk, EPA used a NOAEL of 10 mg/kg/day from a developmental study in rabbits. Because the selected endpoint is from a developmental toxicity study, the sub-population of females, 13-50 years old, is the subgroup of interest. EPA estimates that residues of folpet in diets of females 13-50 years old accounts for 25% of the acute PAD. This leaves 75% of the acute PAD for aggregate risk. The DWLOC corresponding to 75% of the acute PAD is 670 ppb. Because the modeled ground water concentration is only 0.06 ppb and the modeled peak surface water concentration is 156 ppb, aggregate acute exposure and risk are not of concern.

Short and intermediate term aggregate risk estimates do not exceed the Agency's level of concern. Short and intermediate term aggregate risk estimates considered only two potential homeowner exposure scenarios: application of Ready-to-Use paint or stain with either a paint brush or an airless sprayer. The highest exposure, from the airless sprayer, represents a short-term MOE of 407. The chronic dietary exposure from folpet represents less than 1% of the chronic PAD. This leaves 99% of the PAD available for aggregate risk, which corresponds to short-term DWLOC of 228 ppb available for water. The modeled 56-day GENEEC value is 1 ppb, and the modeled concentration of folpet in groundwater is 0.06 ppb. Because the short-term DWLOC is greater than the modeled concentrations of folpet in surface or groundwater, the short-term aggregate risk is not of concern.

In assessing chronic aggregate dietary risk, the Agency used the same exposure assumptions for estimating the chronic (non-cancer) and cancer risk. The drinking water assessment used modeling, as above, to predict ground and surface water concentrations of folpet. Chronic dietary (food) exposure to the US population accounts for less than 1% of the chronic PAD. This leaves 99% of the chronic PAD for aggregate risk. The DWLOC corresponding to 99% of the chronic PAD is 890 ppb, which is far greater than the modeled groundwater concentration of 0.06 ppb and the modeled surface water concentration of 3 ppb. Therefore, the Agency concludes that the aggregate chronic exposure and risk from residues in food and water are not of concern.

Environmental Assessment

Ecological Effects Risk Assessment

The ecological risk assessment and risk mitigation recommendations for folpet are based on the present limited use of folpet. At present, the only potential ecological risks are from the use of folpet on avocados in Florida. Only a very small percentage of Florida avocados are treated with folpet.

Acute and chronic risks to birds and mammals from folpet are not of concern, even at maximum label application rates and frequencies. Folpet also does not appear to pose a risk to honeybees or other insects.

Folpet is highly toxic to most aquatic animal species tested. Based on toxicity test results and results of conservative modeling of folpet concentrations in water, airblast application of folpet to avocados in Florida are expected to exceed high acute risk LOCs for all aquatic animals. Because folpet is applied directly to leaves of avocado trees, only a small amount of folpet will be available for long range spray drift to water. Chronic LOCs are not expected to be exceeded for fish or aquatic invertebrates.

Folpet degrades rapidly in water to the degradates, PI and PAI. The degradate PI has been shown to be only slightly toxic to aquatic animals. No toxicity data are available on PAI. However, since PAI is not expected to be toxicologically significant and usage is limited to two counties in Florida, no additional data will be required at this time. However, if the use pattern changes, the Agency may reconsider this position.

The current spray drift label advisory should be continued. Additional drift mitigation practices may be identified following review of the Spray Drift Task Force database.

A full plant exposure and risk assessment cannot be done with the existing data. Because of the limited use area, no additional data or mitigation are required at this time. However, additional aquatic plant testing would be required with any expansion of folpet use.

Endangered Species

The Agency has concerns about the exposure of threatened and endangered species to folpet. Levels of concern (LOC) are expected to be exceeded for aquatic organisms exposed to single or multiple applications of this fungicide. There are a number of endangered species in avocado growing regions in Florida. These include the Everglades snail kite, whose primary diet consists of apple snails. Although folpet is highly toxic to aquatic invertebrates, such as apple snails, the nearest avocado groves are approximately 3 miles from the Everglades. Therefore, the most likely route of exposure to snails would be long range spray drift, which is unlikely to occur but cannot be quantified at this time. The current spray drift label advisory should be continued. Additional drift mitigation practices may be identified following review of the Spray Drift Task Force database. After its review of the new studies, the Agency will determine whether a reassessment of the potential risks to nontarget organisms is warranted.

Risk Mitigation

To lessen the risks posed by folpet, EPA is requiring the following mitigation measures for folpet-containing products:

- Gloves and dust/mist respirator or equivalent engineering controls are required to lessen the risks to workers adding the wettable powder to paints and stains during the manufacturing process; and

- An Environmental Hazard warning is required to lessen risks to nontarget aquatic organisms. Specific label language is provided in Section V of the RED.

Additional Data Required

EPA is requiring the following additional generic studies for folpet to confirm its regulatory assessments and conclusions:

Guideline 830.7050,UV/Visible Absorption for the PAI

Guideline 860.1200, Direction for Use

Guideline 860.1380, Storage Stability for avocados, cucumber, and melon

Guideline 860.1480, Magnitude of the Residue in Meat and Milk (Ruminant Feeding Study)

Guideline 850.1300, Chronic *Daphnia* Toxicity

Guideline 870.3700, Prenatal Developmental Toxicity in the New Zealand White Rabbit

Guideline 875(series), Exposure Monitoring for application with wood dip and paint roller.

These data are confirmatory; i.e., they are not expected to change the conclusions of this RED.

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 folpet 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 folpet RED document.

PPE for workers adding wettable powder to sealants and coatings during manufacturing process: Chemical resistant gloves and a dust/mist respirator are required. If available, engineering controls such as closed loading systems are an adequate substitute for the PPE.

REI: Since folpet is in toxicity category II for inhalation exposure and eye irritation, a 24-hour restricted entry interval (REI) is required for avocado harvesters. Early entry PPE is required for any workers who enter treated avocado orchards before the 24-hour REI.

Environmental Hazard Statement: "This chemical is highly toxic to fish and other aquatic organisms. Do not apply directly to water. Do not contaminate water when disposing of equipment, washwater, or rinsate."

Regulatory Conclusion

The use of currently registered products containing folpet in accordance with approved labeling will not pose unreasonable risks or adverse effects to humans or the environment. Therefore, the Agency has determined that all supported folpet products are eligible for reregistration under the conditions specified in this RED. Products containing folpet for use on avocados and in coatings and sealants are eligible for reregistration. As mentioned previously, the registrants are not supporting other folpet uses and have requested voluntary cancellation of agricultural, ornamental, and greenhouse registrations (EPA Registration numbers

66222-8 and 7401-231). These unsupported uses were suspended due to lack of supporting data and are ineligible for reregistration.

Folpet 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 folpet 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 Center for Environmental Publications and Information (EPA/NCEPI), PO Box 42419, Cincinnati, OH 45242-2419, telephone 1-800-490-9198; fax 513-489-8695.

Following the comment period, the folpet 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 folpet RED, or reregistration of individual products containing folpet, 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 Pesticide Telecommunications Network (NPTN). 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 ace.orst.edu/info/nptn.