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United States
Environmental Protection
Agency

Prevention, Pesticides
and Toxic Substances
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Report of the Food Quality Protection Act (FQPA) Tolerance Reassessment Progress and Risk Management Decision (TRED) for Fluridone

US EPA ARCHIVE DOCUMENT



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

CERTIFIED MAIL

Dear Registrant:

This is the Environmental Protection Agency's (hereafter referred to as EPA or the Agency) "Report of the Food Quality Protection Act (FQPA) Tolerance Reassessment Progress and Risk Management Decision for Fluridone," which was approved on September 20, 2004. This document is also known as a Tolerance Reassessment Decision, or TRED. A Notice of Availability of this tolerance reassessment decision will be published shortly.

The Federal Food, Drug and Cosmetic Act (FFDCA), as amended by FQPA, requires EPA to reassess all the tolerances for registered chemicals in effect on or before the enactment of the FQPA on August 3, 1996. In reassessing these tolerances, the Agency must consider, among other things, aggregate risks from non-occupational sources of pesticide exposure, whether there is increased susceptibility to infants and children, and the cumulative effects of pesticides with a common mechanism of toxicity. Once a safety finding has been made, the tolerances are considered reassessed. Existing tolerances associated with fluridone must be reassessed in accordance with FFDCA, as amended by FQPA.

The Agency has evaluated all current registered uses of fluridone and has determined that there is a reasonable certainty that no harm to any population subgroup will result from exposure when considering dietary exposure and all other non-occupational sources of pesticide exposure for which there is reliable information. The food, drinking water and recreational swimmer risks are not of concern separately or when aggregated. Therefore, no mitigation measures are needed, and the current tolerances established at 40 CFR 180.420 for residues of fluridone in/on raw agricultural commodities are now considered reassessed as safe under section 408(q) of the FFDCA.

Fluridone is a systemic herbicide that is used to manage aquatic weeds in ponds and lakes. It is particularly useful for the control of hydrilla in the southern states and eurasian milfoil in the northern states. It inhibits carotene synthesis which causes the loss of chlorophyll. It is typically applied to the whole water body because it requires a contact time of 45 days to be effective. The labels permit single treatments of up to 90 ppb for whole lake treatments and 150 ppb for partial lake treatments, with a maximum cumulative application of 150 ppb per growth cycle. There are no direct food uses for fluridone, however, water from areas treated with fluridone can be used for the irrigation of crops and pastures.

Fluridone is a Toxicity Category III for acute dermal and eye irritation, and Toxicity Category IV for acute oral, acute inhalation and dermal irritation. It is not a dermal sensitizer. There was no indication of reproductive or neurotoxicant effects from fluridone in the reviewed studies. Fluridone is classified as not likely to be carcinogenic to humans.

Residential Margin of Exposures (MOEs) greater than 100 are not of concern to the Agency. The MOE of 100 is based on the standard safety factor of 10X for intraspecies variability (i.e. differences among humans) and 10X for interspecies variability (differences between humans and animals). Additional factors for database uncertainties were not required because the database was considered complete and there were no datagaps.

The FQPA Safety Factor was reduced to 1X, based on the available hazard and exposure data. It is applicable to all population subgroup and exposure scenarios. There was no evidence of pre- or post-natal susceptibility from *in utero* or postnatal exposure to fluridone and there are no residual uncertainties.

N-methyl Formamide (NMF) is the major degradate when fluridone is applied to water bodies. A limited number of studies have been conducted under field conditions and these studies suggest that NMF is undetectable in water bodies treated with fluridone at the maximum application rate. The toxicology database for NMF is limited to one developmental study that was reported in the literature. NMF is not a metabolite in foods.

Fluridone acute and chronic dietary exposure assessments were conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCIDtm, Version 1.30) and the Lifeline Model Version 2.0 which uses food consumption data from USDA's Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. The acute dietary risk estimates were calculated only for females of child-bearing age (13-49), as an appropriate endpoint for the general population was not identified. The acute dietary exposure estimates are less than 1% of the aPAD. For the acute dietary exposure assessment a developmental no observed adverse effect level (NOAEL) of 125 mg/kg/day was selected from a developmental toxicity study in rabbits in which increased incidences of abortions was observed at the lowest observed adverse effect level (LOAEL) of 300 mg/kg/day. The chronic dietary risk estimates were calculated for all population subgroups. The chronic dietary exposure estimates ranged from 1% of the cPAD for the general U.S. population to 3.6% of the cPAD for children ages 1-2. For the chronic dietary exposure assessment a NOAEL of 15 mg/kg/day was selected from a 2-year carcinogenicity study in mice in which increased alkaline phosphatase activity and hepatocellular hyperplasia was observed at the LOAEL of 50 mg/kg/day. All acute and chronic dietary exposure estimates from fluridone are less than 3.6% of the PAD and are below the Agency's level of concern.

The drinking water risk were calculated for both fluridone and its major degradate NMF because fluridone degrades to NMF in water. The drinking water MOEs for fluridone are ≥ 7500 and exceed the target MOE of 100. All drinking water exposures are below the Agency's level of concern.

There is a possibility that swimmer exposures could occur following fluridone applications to recreational lakes. The recreational swimmer exposure estimates were evaluated using the SWIMODEL and standard assumptions from the residential SOPs. The swimmer MOEs are $\geq 4,800$ and exceed the target MOE of 100. All swimmer exposure estimates are below the Agency's level of concern.

Aggregate risk has been calculated for fluridone and the degradate NMF by combining the food, drinking water, and residential exposures (recreation swimmers). The acute aggregate exposures for food, drinking water and recreational swimmers were calculated only for females because the acute dietary endpoint is based on developmental effects and only applies to females. Short- and intermediate-term aggregate exposures for food, drinking water and recreational swimmers were calculated for adults and children ages 1 to 6. Chronic aggregate exposures were calculated for food and drinking water for all population sub-groups because the swimmer exposure does not occur on a long term basis. All of the aggregate risks from dietary, drinking water including metabolites, and recreational exposures to fluridone are below the Agency's level of concern and no risk mitigation is required.

FQPA requires that EPA consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." The Agency considers other substances because low-level exposures to multiple chemical substances that cause a common toxic effect by a common mechanism could lead to the same adverse health effect, as would a higher level of exposure to any of the other substances individually.

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to fluridone and any other substances and fluridone does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that fluridone has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at: <http://www.epa.gov/pesticides/cumulative/>.

EPA is required under the FFDCFA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific bases for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCFA authority to require the wildlife evaluations. As the science develops and

resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

In the available toxicity studies on fluridone, there were no estrogen, androgen and/or thyroid mediated toxicity. When the appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, fluridone may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

Tolerance Reassessment

All of the existing fluridone tolerances established at 40 CFR 180.420 are adequately supported and are considered reassessed by the Agency. These tolerances are listed in Table 1.

Table 1. Reassessed Tolerances for Fluridone That Were Included in the Dietary Risk Assessments			
Commodity	Tolerance (ppm)	Commodity	Tolerance (ppm)
Avocado	0.1	Hog, Meat by-products	0.05
Cattle, Fat	0.05	Hops	0.1
Cattle, Kidney	0.1	Horse, Fat	0.05
Cattle, Liver	0.1	Horse, Kidney	0.1
Cattle, Meat, except Kidney and Liver	0.05	Horse, Liver	0.1
Cattle, Meat by-products	0.05	Horse, Meat, except Kidney and Liver	0.05
Citrus	0.1	Horse, Meat by-products	0.05
Cotton, Undelinted Seed	0.1	Leafy vegetables	0.1
Crayfish	0.5	Legume, forage	0.15
Cucurbit vegetables group	0.1	Milk	0.05
Egg	0.05	Nut	0.1
Fish	0.5	Poultry, Fat	0.05
Fruit, Pome	0.1	Poultry, Kidney	0.01
Fruit, Stone	0.1	Poultry, Liver	0.01
Goat, Fat	0.05	Poultry, Meat, except Kidney and Liver	0.05
Goat, Kidney	0.1	Poultry, Meat by-products	0.05
Goat, Liver	0.1	Root Crop Vegetables	0.1
Goat, Meat, except Kidney and Liver	0.05	Seed and Pod Vegetables	0.1
Goat, Meat by-products	0.05	Sheep, Fat	0.05
Grain, crop	0.1	Sheep, Kidney	0.1
Grass, Forage	0.15	Sheep, Liver	0.1
Hog, Fat	0.05	Sheep, Meat, except Kidney and Liver	0.05
Hog, Kidney	0.1	Sheep, Meat by-products	0.05
Hog, Liver	0.1	Small Fruit	0.1
Hog, Meat, except Kidney and Liver	0.05	Vegetables, fruiting	0.1

This document summarizes the Agency's decision on the tolerance reassessment for fluridone. Please contact Wilhelmena Livingston of my staff with any questions regarding this decision; she may be reached by phone at (703) 308-8025 or by e-mail at livingston.wilhelmena@epa.gov.

Sincerely,

Debbie Edwards, Ph.D.
Director
Special Review and Reregistration Division

Enclosures: *Human Health Risk Assessment for Fluridone TRED.*

Fluridone and its Major Degradate, N-methyl formamide – Drinking Water Assessment for the Health Effects Division (HED) Reregistration Eligibility Decision Document.

Fluridone: Toxicology Chapter for TRED.

Fluridone Acute and Chronic Dietary Exposure Assessments for the Reregistration Eligibility Decision.