



**UNITED STATES ENVIRONMENTAL PROTECTION AGENCY**

**WASHINGTON, D.C. 20460**

**OFFICE OF  
PREVENTION, PESTICIDES  
AND TOXIC SUBSTANCES**

**MEMORANDUM**

DATE: August 12 , 2004

SUBJECT: **Fluridone** Acute and Chronic Dietary Exposure Assessments for the Reregistration Eligibility Decision

PC Code: 112900  
DP Barcode: D299947

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**Executive Summary**

Acute and chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM-FCID™, Version 1.30), and the Lifeline Model Version 2.0 which uses food consumption data from the USDA's Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. The analyses were performed to support the reregistration

eligibility decision.

An acute analysis was conducted only for females 13-49, as an appropriate endpoint for the general population was not identified. The acute and chronic analyses were conducted using tolerance level residues and assumed all commodities were treated. At the 95<sup>th</sup> percentile of exposure for the acute analysis for females 13-49 yrs, the exposure was <1% of the population adjusted dose (aPAD). For the chronic analysis the most highly exposed population subgroup was children 1-2 yrs with an exposure estimate of 4% of the cPAD, while the estimate for the general population was 1% of the cPAD. Chronic and acute analyses were conducted using both DEEM-FCID™ (Version 1.30) and Lifeline™ (Version 2.0); results from both analyses were consistent. These analyses are conservative so the actual exposure is likely lower than the estimates provided herein.

## **I. Introduction**

Dietary risk assessment incorporates both exposure and toxicity of a given pesticide. For acute and chronic assessments, the risk is expressed as a percentage of a maximum acceptable dose (i.e., the dose which HED has concluded will result in no unreasonable adverse health effects). This dose is referred to as the population adjusted dose (PAD). The PAD is equivalent to the Reference Dose (RfD) divided by the special FQPA Safety Factor.

For acute and non-cancer chronic exposures, HED is concerned when estimated dietary risk exceeds 100% of the PAD. References which discuss the acute and chronic risk assessments in more detail are available on the EPA/pesticides web site: “Available Information on Assessing Exposure from Pesticides, A User’s Guide,” 6/21/2000, web link: <http://www.epa.gov/fedrgstr/EPA-PEST/2000/July/Day-12/6061.pdf> ; or see SOP 99.6 (8/20/99).

The most recent dietary risk assessment for fluridone was conducted in 1986 when the tolerances were first established.

## **II. Residue Information**

Fluridone is an aquatic herbicide used to kill various weeds in water bodies. Fluridone is not applied directly to crops or livestock, but treated water may be used to irrigate food and feed crops or fed to livestock. Tolerances have been established in 40 CFR § 180.420 for virtually all crop groups and a few crops that are not included in any group.

Tolerance values listed in Table 1 were used in the acute and chronic dietary exposure assessments with no refinements for percent crop treated. The default processing factors in DEEM™ Version 7.76 were also used. Most tolerances are set at twice the limit of quantitation of the analytical method. The US Pesticide Data Program analyzed for residues of fluridone in/on 5,248 samples during 2001 and 2000. Fluridone *per se* has never been detected at limits of

detection generally ranging from 0.013 to 0.035 ppm.

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

### III. Program and Consumption Information

Several reasonable peer-reviewed softwares have recently been emerging for modeling dietary exposure to pesticides. For a variety of technical, historical, and availability reasons, DEEM-FCID™ was the program generally used by EPA’s Office of Pesticide Programs for conducting its dietary risk assessments. With the advent and current availability of a number of other exposure software programs, OPP, registrants, and other interested parties have available to them the

option of selecting other peer-reviewed exposure software in conducting risk assessments for pesticides. Lifeline™ is one such model and is also being used in this HED review. Dietary Exposure assessments may also be performed with other, similar programs, and if submitted, such results will be reviewed by EPA for acceptability and comparability to existing peer-reviewed software being used by OPP.

### **IIIa. DEEM-FCID™ Program and Consumption Information**

Fluridone acute and chronic dietary exposure assessments were conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™, Version 1.30), which incorporates consumption data from USDA's Continuing Surveys of Food Intakes by Individuals (CSFII), 1994-1996 and 1998. The 1994-96, 98 data are based on the reported consumption of more than 20,000 individuals over two non-consecutive survey days. Foods "as consumed" (e.g., apple pie) are linked to EPA-defined food commodities (e.g. apples, peeled fruit - cooked; fresh or N/S; baked; or wheat flour - cooked; fresh or N/S, baked) using publicly available recipe translation files developed jointly by USDA/ARS and EPA. For chronic exposure assessment, consumption data are averaged for the entire U.S. population and within population subgroups, but for acute exposure assessment are retained as individual consumption events. Based on analysis of the 1994-96, 98 CSFII consumption data, which took into account dietary patterns and survey respondents, HED concluded that it is most appropriate to report risk for the following population subgroups: the general U.S. population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, adults 20-49, females 13-49, and adults 50+ years old.

For chronic dietary exposure assessment, an estimate of the residue level in each food or food-form (e.g., orange or orange juice) on the food commodity residue list is multiplied by the average daily consumption estimate for that food/food form to produce a residue intake estimate. The resulting residue intake estimate for each food/food form is summed with the residue intake estimates for all other food/food forms on the commodity residue list to arrive at the total average estimated exposure. Exposure is expressed in mg/kg body weight/day and as a percent of the cPAD. This procedure is performed for each population subgroup.

For acute exposure assessments, individual one-day food consumption data are used on an individual-by-individual basis. The reported consumption amounts of each food item can be multiplied by a residue point estimate and summed to obtain a total daily pesticide exposure for a deterministic exposure assessment, or "matched" in multiple random pairings with residue values and then summed in a probabilistic assessment. The resulting distribution of exposures is expressed as a percentage of the aPAD on both a user (i.e., only those who reported eating relevant commodities/food forms) and a per-capita (i.e., those who reported eating the relevant commodities as well as those who did not) basis. However, for tiers 1 and 2, any significant differences in user vs. per capita exposure and risk are specifically identified and noted in the risk assessment.

### **IIIb. Lifeline™ Program and Consumption Information**

Acute and chronic dietary exposure estimates were also conducted using the Lifeline™ model (Version 2.0). These Lifeline™ assessments were also conducted using the same consumption data as the DEEM-FCID™ (CSFII, 1994-1996 and 1998 consumption data with FCID). Lifeline™ uses the recipe file to relate RACs to foods “as-eaten.” Lifeline™ converts the RAC residues into food residues by randomly selecting a RAC residue value from the “user defined” residue distribution (created from the residue, percent crop treated, and processing factors data), and calculating a net residue for that food based on the ingredients’ mass contribution to that food item. For example, ‘apple pie’ will have a residue distribution based on the residues provided for apples (adjusted by the appropriate processing factors and percent crop treated), as well as the residues for each of the other ingredients in the apple pie recipe for which there may be tolerances. Lifeline™ calculates dietary exposure from ‘apple pie’ based on the amount eaten, and the residue drawn from the ‘apple pie’ residue distribution for that eating occasion.

Lifeline™ models the individual’s dietary exposures over a season by selecting a new CSFII diary each day from a set of similar individuals based on age and season attributes. Lifeline™ groups CSFII diaries based on the respondents’ age and the season during which the food diary was recorded. Further information regarding the Lifeline™ model can be found at the following web site: [www.theLifeline™group.org](http://www.theLifeline™group.org).

## **IV. Toxicological Information**

The doses and endpoints selected for use in the dietary assessments were selected by a team of toxicologists in Reregistration Branch I, Health Effects Division (B. Chin, DP Barcode D291522, 6/10/04, TXR. No. 0052046). The database is substantially complete, and no concerns were identified that would necessitate a hazard-based special FQPA safety factor.

Table 2. Summary of Toxicological Doses and Endpoints for Fluridone for Use in Dietary Exposure Assessment			
Exposure Scenario	Dose Used in Risk Assessment, UF	Hazard and Exposure Based Special FQPA Safety Factor	Study and Toxicological Effects
Acute Dietary (General population including infants and children)	NOT APPLICABLE. A dose and endpoint were not selected for this population group because there were no effects observed in oral toxicology studies including maternal toxicity in the developmental toxicity studies in rats and rabbits that are attributable to a single exposure (dose).		
Acute Dietary (Females 13-50 years of age)	Dev. NOAEL = 125 mg/kg/day UF = 100 Acute RfD = 1.25 mg/kg/day	FQPA SF = 1X aPAD = $\frac{\text{acute RfD}}{\text{FQPA SF}}$ = 1.25mg/kg/day	Developmental Toxicity - Rabbit LOAEL = 300 mg/kg/day based on increased incidences of abortions
Chronic Dietary (All populations)	NOAEL= 15 mg/kg/day UF =100 Chronic RfD = 0.15 mg/kg/day	FQPA SF = 1X cPAD = $\frac{\text{chronic RfD}}{\text{FQPA SF}}$ = 0.15 mg/kg/day	2 yr. cancer study in mice LOAEL =50 mg/kg/day based on increased phosphatase activity and increased incidence of hepatocellular hyperplasia

## V. Results/Discussion

As stated above, for acute and chronic assessments, HED is concerned when dietary risk exceeds 100% of the PAD. The DEEM-FCID™ analyses estimate the dietary exposure of the U.S. population and various population subgroups. The results reported in Table 3 for the acute and chronic assessments are for the general U.S. Population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, females 13-49, adults 20-49, and adults 50+ years. Acute risks were determined only for females of childbearing age, and are less than 1% of the aPAD. The most highly exposed sub-population was children aged 1-2, with a risk estimate of 3.6 % of the cPAD. These exposures are all well below 100% of the PAD and are not of concern.

Acute and chronic dietary risks were also estimated using the Lifeline™ model (version 2.0). The Lifeline™ model estimated acute exposure based on the acute 1-day dietary dose drawn randomly from an age-specific seasonal exposure profile of 5000 individuals. The Lifeline™ chronic dietary exposure estimate is based on an average daily exposure from a profile of 5000 individuals over a one year period. Results of the Lifeline™ analysis are fully consistent with DEEM-FCID™ results. The Lifeline™ model estimate for the 95th percentile acute dietary exposure for females ages 13-49 is less than 1% of the aPAD. The Lifeline™ chronic dietary exposure estimate for 1-2 year olds is 3.5% of the cPAD.

<b>Table 3. Summary of Dietary Exposure and Risk for Fluridone</b>				
Population Subgroup	Dietary Exposure (mg/kg/day)		% PAD <sup>1</sup>	
	DEEM-FCID™	Lifeline™	DEEM-FCID™	Lifeline™
<b>Chronic Assessment</b>				
General U.S. Population	0.001599	0.001514	1.1	1.0
All Infants (< 1 year old)	0.002661	0.002545	1.8	1.7
<b>Children 1-2 years old</b>	<b>0.005345</b>	<b>0.005181</b>	<b>3.6</b>	<b>3.5</b>
Children 3-5 years old	0.004123	0.004043	2.7	2.7
Children 6-12 years old	0.002529	0.002339	1.7	1.6
Youth 13-19 years old	0.001454	0.001341	1.0	0.9
Adults 20-49 years old	0.001154	0.001218	0.8	0.8
Adults 50+ years old	0.001074	0.001191	0.7	0.8
Females 13-49 years old	0.001134	0.001377	0.8	0.9
<b>Acute Assessment</b>				
<b>Females 13-49 years old</b>	<b>0.002352</b>	<b>0.003009</b>	<b>0.19</b>	<b>0.24</b>

<sup>1</sup> HED is generally not concerned if the %PAD is less than 100%.

## VI. Characterization of Inputs/Outputs

The dietary exposures estimated in this analysis are likely higher than actual exposures to fluridone. Tolerance level residues were used, but monitoring and field trial data generally show non-detectable residues on most foods. In addition, this analysis assumes all foods were treated; only a small percentage of crops grown would likely be irrigated with water from treated sources. Accordingly, this analysis can be characterized as very conservative.

## VII. Conclusions

Acute and chronic exposure estimates for all population sub-groups are well below the level of concern. This assessment is conservative and assumes tolerance level residues and all crops are treated. Actual exposure is likely to be lower than the values provided in this analysis.

**VIII. List of Attachments**

- Acute Food Residue Input file.
- Acute Results file
- Chronic Food Residue Input file.
- Chronic Results file.

cc: Colinger, SRRD.