

Fluopicolide  
PC Code: 027412

Dietary Exposure and Risk Assessment

DP Number: 334710



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF  
PREVENTION, PESTICIDES  
AND TOXIC SUBSTANCES

MEMORANDUM

DATE: 31-JAN-2007

SUBJECT: **Fluopicolide** Chronic Dietary (Food Only) Exposure and Risk Assessment  
for the Section 3 Action on Imported Grapes and Raisins

PC Code: 27412  
DP Number: 334710

Decision Number: 353910

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## Executive Summary

A chronic dietary (food only) exposure and risk assessment was conducted using the Dietary Exposure Evaluation Model DEEM-FCID™, Version 2.03, which uses food consumption data from the U.S. Department of Agriculture's Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. The analysis was performed to support permanent tolerances for fluopicolide residues on imported grapes and raisins.

**This assessment is for fluopicolide (parent) only. 2,6-Dichlorobenzamide (BAM) is a metabolite and/or environmental degradate of both fluopicolide and dichlobenil. As determined by the HED Risk Assessment Review Committee (RARC1) on 12/21/06, BAM will not be included in the tolerance or risk assessment for fluopicolide on imported grapes because 1) as both a plant and rat metabolite of fluopicolide, it has been included in the toxicology studies and fluopicolide endpoint selections; and 2) residues of BAM in food resulting from fluopicolide on imported grapes is expected to be negligible since BAM is only 2.0% of the total radioactive residue in the fluopicolide grape metabolism study and is a maximum of only 0.047 ppm in the fluopicolide grape field trials. However, both parent fluopicolide and BAM will be included in risk assessments for future uses of fluopicolide on domestic crops since more exposure to BAM is expected with domestic uses.**

**This assessment is for fluopicolide on food only. No exposure will occur from drinking water as a result of residues of fluopicolide on imported grapes and raisins.**

### Chronic Dietary (Food Only) Exposure Results and Characterization

The results of the chronic dietary (food only) exposure analysis which was conducted for fluopicolide residues on imported grapes and raisins are reported in Table 3 below. A conservative (Tier 1) assessment was conducted. The residue levels used in the assessment were the recommended tolerance levels of 2.0 ppm for grapes and 6.0 ppm for raisins. An adequate processing study was conducted on grapes indicating no concentration in grape juice but concentration in raisins. No default processing factors were used since an adequate processing study was available. Since no livestock feed items are associated with grapes, no residues are expected to occur in livestock commodities. The assessment assumed that 100% of the crop was treated and 100% of the crop was imported.

The chronic dietary (food only) exposure to fluopicolide is below HED's level of concern for the general U.S. population and all population subgroups. The chronic dietary exposure estimates are <1% cPAD for the general U.S. population and 3% cPAD for children 1-2 years old, the most highly exposed subgroup.

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## 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 point of departure (POD, NOAEL, LOAEL, e.g.) divided by the required uncertainty or safety factors.

For acute and non-cancer chronic exposures, HED is concerned when estimated dietary risk exceeds 100% of the PAD. HED is generally concerned when estimated cancer risk exceeds one in one million. 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," 21-JUN-2000, web link: <http://www.epa.gov/fedrgstr/EPA-PEST/2000/July/Day-12/6061.pdf>; or see SOP 99.6 (20-AUG-1999).

This is the first dietary risk assessment for fluopicolide.

## II. Residue Information

### Fluopicolide on Imported Grapes and Raisins:

No tolerances have been established for fluopicolide. HED is presently recommending for the following tolerances for fluopicolide (parent):

Grape	2.0 ppm
Grape, raisin	6.0 ppm

The residue of concern for the tolerance expression is fluopicolide (parent). The residue of concern for this risk assessment on imported grapes only is fluopicolide (parent) only. 2,6-Dichlorobenzamide (BAM) is a metabolite and/or environmental degradate of both fluopicolide and dichlobenil. As determined by the HED Risk Assessment Review Committee (RARCI) on 21-DEC-2006, BAM will not be included in the tolerance or risk assessment for fluopicolide on imported grapes because 1) as both a plant and rat metabolite of fluopicolide, it has been included in the toxicology studies and fluopicolide endpoint selections; and 2) residues of BAM in food resulting from fluopicolide on imported grapes is expected to be negligible since BAM is only 2.0% of the total radioactive residue in the fluopicolide grape metabolism study and is a maximum of only 0.047 ppm in the fluopicolide grape field trials. However, both parent fluopicolide and BAM will be included in risk assessments for future uses of fluopicolide on domestic crops since more exposure to BAM is expected with domestic uses.

This assessment is for fluopicolide on food only. No exposure is expected to occur from drinking water as a result of residues of fluopicolide on imported grapes and raisins.

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Matrix		Residues included in Risk Assessment	Residues included in Tolerance Expression
Imported Grapes	Primary Crop	fluopicolide <i>per se</i> <sup>1</sup>	fluopicolide <i>per se</i>
	Rotational Crop	Not applicable for an import <sup>2</sup>	Not applicable for an import <sup>2</sup>
Livestock	Ruminant	Not applicable since no livestock feedstuffs are associated with grapes. <sup>2,3</sup>	Not applicable since no livestock feedstuffs are associated with grapes. <sup>2,3</sup>
	Poultry		
Drinking Water		Not applicable for an import	Not applicable

<sup>1</sup> The risk assessment for domestic crops will include both fluopicolide (parent) and 2,6-dichlorobenzamide (BAM).

<sup>2</sup> HED SOP 98.6, *Data Requirements for Import Tolerances*, Table 3, 03-DEC-1998.

<sup>3</sup> OPPTS 860.1000, Table 1 Feedstuffs (October 2006)

#### Residue Data used for the Chronic Assessment:

The recommended tolerance level residues of 2.0 ppm for grapes and 6.0 ppm for raisins were used. An adequate processing study was conducted on grapes indicating no concentration in grape juice but concentration in raisins (DP Number 321209, A. Acierto, 23-JAN-2007). Since residues of fluopicolide do not concentrate in juice, 2.0 ppm was also used for grape juice and wine. No default processing factors were used since an adequate processing study was available. Since no livestock feed items are associated with grapes, no residues are expected to occur in livestock commodities. It was assumed that 100% of the crop was treated and 100% of the crop was imported.

### **III. Drinking Water Data**

No residues are expected to occur in drinking water as a result of residues on imported crops.

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

A fluopicolide chronic dietary exposure assessment was conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database DEEM-FCID™, Version 2.03, 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

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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.

## **V. Toxicological Information**

The Fluopicolide Risk Assessment Team selected endpoints for this new pesticide. The Fluopicolide CARC was held on 15-NOV-2006. An HED metabolism assessment meeting was held on 07-DEC-2006. The RARC was held on 21-DEC-2006.

It is recommended that the 10X FQPA safety factor for the protection of infants and children be removed. Developmental toxicity was found in rats and rabbits, in the presence of maternal toxicity; however, there is low concern for qualitative susceptibility. In addition, the data base is adequate and although there was not a developmental neurotoxicity study, evidence from other studies indicate that one is not required. The acute and subchronic neurotoxicity studies showed no gross or microscopic brain pathology associated with this test substance, and none of the studies indicated any clinical signs of toxicity that would be associated with neurological function.

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<b>Exposure/Scenario</b>	<b>Point of Departure</b>	<b>Uncertainty/FQPA Safety Factors</b>	<b>RfD, PAD, Level of Concern</b>	<b>Study and Toxicological Effects</b>
Acute Dietary (General Population, including Infants and Children)	None	None	None	<b>An appropriate endpoint was not identified from the available data.</b>
Chronic Dietary (All Populations)	Maternal NOAEL=20 mg/kg/day	UF <sub>A</sub> =10x UF <sub>H</sub> =10x	Chronic RfD = 0.20 mg/kg/day  cPAD = 0.20 mg/kg/day	<b>Developmental Toxicity Study in Rabbits</b> LOAEL =60 mg/kg/day based on death, abortions/premature deliveries, decreased food consumption, decreased body weight gain.
Cancer (oral, dermal, inhalation)	Classification: "Not likely to be carcinogenic to humans."			

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF<sub>A</sub> = extrapolation from animal to human (interspecies). UF<sub>H</sub> = potential variation in sensitivity among members of the human population (intraspecies). FQPA SF = FQPA Safety Factor. PAD = population adjusted dose (a = acute, c = chronic). RfD = reference dose.

## VI. Results/Discussion

As stated above, for the chronic assessment, 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 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.

**This assessment is for fluopicolide (parent) on food only. No exposure is expected to occur from drinking water as a result of residues of fluopicolide on imported grapes and raisins.**

### Results of Chronic Dietary (Food Only) Exposure Analysis

The results of the chronic dietary (food only) exposure assessment which was conducted for residues of fluopicolide on imported grapes and raisins are reported in Table 3 below. A conservative (Tier 1) assessment was conducted. The residue levels used in the assessment were the recommended tolerance levels of 2.0 ppm for grapes and 6.0 ppm for raisins. An adequate processing study was conducted on grapes indicating no

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concentration in grape juice but concentration in raisins. No default processing factors were used since an adequate processing study was available. Since no livestock feed items are associated with grapes, no residues are expected to occur in livestock commodities. The assessment assumed that 100% of the crop was treated and 100% of the crop was imported.

The chronic dietary (food only) exposure to fluopicolide is below HED's level of concern for the general U.S. population and all population subgroups. The chronic dietary exposure estimates are <1% cPAD for the general U.S. population and 3% cPAD for children 1-2 years old, the most highly exposed subgroup.

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Population Subgroup	Acute Dietary		Chronic Dietary		Cancer	
	Dietary Exposure (mg/kg/day)	% aPAD	Dietary Exposure (mg/kg/day)	% cPAD	Dietary Exposure (mg/kg/day)	Risk
General U.S. Population	N/A	N/A	0.001129	<1	N/A	N/A
All Infants (< 1 year old)			0.001742	<1		
Children 1-2 years old			<b>0.006272</b>	<b>3</b>		
Children 3-5 years old			0.003827	2		
Children 6-12 years old			0.001456	<1		
Youth 13-19 years old			0.000513	<1		
Adults 20-49 years old			0.000697	<1		
Adults 50+ years old			0.000828	<1		
Females 13-49 years old			0.000748	<1		

\* No exposure is expected to occur from drinking water as a result of fluopicolide residues on imported grapes and raisins.

## VII. Characterization of Inputs/Outputs

A conservative (Tier 1) chronic dietary (food only) exposure assessment was conducted. The residue levels used in the chronic assessment for imported grapes and raisins were the recommended tolerance levels of 2.0 ppm for grapes and 6.0 ppm for raisins. An adequate processing study was conducted on grapes indicating no concentration in grape juice but concentration in raisins. No default processing factors were used since an adequate processing study was available. Since no livestock feed items are associated with grapes, no residues are expected to occur in livestock commodities. The assessment assumed 100% of the crop was treated and 100% of the crop was imported. No exposure is expected to occur from drinking water as a result of residues on imported crops. Although not needed at this time, HED could refine the exposure and risk estimates with the following information: 1) projected market share/percent crop treated data; and 2) anticipated residue data.

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## **VIII. Conclusions**

A chronic dietary (food only) exposure assessment was conducted for the proposed use on imported grapes. A conservative (Tier 1) assessment was conducted using tolerance level residues and assuming 100% of the crop was treated and 100% of the crop was imported. No exposure is expected to occur from drinking water as a result of residues on imported crops.

The chronic dietary (food only) exposure to fluopicolide is below HED's level of concern for the general U.S. population and all population subgroups. The chronic dietary exposure estimates are <1% cPAD for the general U.S. population and 3% cPAD for children 1-2 years old, the most highly exposed subgroup.

## **IX. List of Attachments**

1. Chronic Food Only Residue Input File
2. Chronic Food Only Results File

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### Attachment 1: Chronic Food Only Residue Input File

Filename: C:\Documents and Settings\NDODD\My Documents\DEEMFCIDNDODD\Fluopicolide\fluopicolidegrape010307.R98  
 Chemical: fluopicolide  
 RfD(Chronic): 12 mg/kg bw/day NOEL(Chronic): 0 mg/kg bw/day  
 RfD(Acute): 0 mg/kg bw/day NOEL(Acute): 0 mg/kg bw/day  
 Date created/last modified: 01-03-2007/16:47:00/8 Program ver. 2.03

EPA Code	Crop Grp	Commodity Name	Def Res (ppm)	Adj.Factors #1	Adj.Factors #2	Comment
95001750	0	Grape	1.000000	1.000	1.000	
95001760	0	Grape, juice	2.000000	1.000	1.000	
95001761	0	Grape, juice-babyfood	2.000000	1.000	1.000	
95001780	0	Grape, raisin	6.000000	1.000	1.000	
95001790	0	Grape, wine and sherry	1.000000	1.000	1.000	

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## Attachment 2: Chronic Food Only Results File

U.S. Environmental Protection Agency Ver. 2.00  
DEEM-FCID Chronic analysis for FLUCPICOLIDE (1994-98 data)  
Residue file name: C:\Documents and Settings\NDODD\My  
Documents\DEEMFCIDNDODD\Fluopicolide\fluopicolidegrape010307.R98  
Adjustment factor #2 NOT used.

Analysis Date 01-03-2007/16:49:07 Residue file dated: 01-03-2007/16:47:00/8  
Reference Dose (RfD, Chronic) = .2 mg/kg bw/day

=====  
Total exposure by population subgroup  
=====

Population Subgroup	Total Exposure	
	mg/kg body wt/day	Percent of Rfd
U.S. Population (total)	0.001129	0.6%
U.S. Population (spring season)	0.001075	0.5%
U.S. Population (summer season)	0.001222	0.6%
U.S. Population (autumn season)	0.001079	0.5%
U.S. Population (winter season)	0.001139	0.6%
Northeast region	0.001346	0.7%
Midwest region	0.001113	0.6%
Southern region	0.000969	0.5%
Western region	0.001204	0.6%
Hispanics	0.000881	0.4%
Non-hispanic whites	0.001213	0.6%
Non-hispanic blacks	0.000969	0.5%
Non-hispanic-white/non-black	0.000793	0.4%
All infants (< 1 year)	0.001742	0.9%
Nursing infants	0.000665	0.3%
Non-nursing infants	0.002151	1.1%
Children 1-5 yrs	0.004319	2.2%
Children 6-12 yrs	0.001378	0.7%
Females 13-19 (not preg or nursing)	0.000609	0.3%
Females 20- (not preg or nursing)	0.000822	0.4%
Females 13-50 yrs	0.000780	0.4%
Females 13- (preg/not nursing)	0.000453	0.2%
Females 13- (nursing)	0.000675	0.3%
Males 13-19 yrs	0.000421	0.2%
Males 20- yrs	0.000669	0.3%
Seniors 65+	0.000850	0.4%
Children 1-5 yrs	0.006272	3.1%
Children 6-12 yrs	0.003827	1.9%
Children 13-12 yrs	0.001456	0.7%
South 13-19 yrs	0.000513	0.3%
Adults 30-49 yrs	0.000697	0.3%
Adults 50- yrs	0.000828	0.4%
Females 13-49 yrs	0.000748	0.4%



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