



## UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF  
PREVENTION, PESTICIDES  
AND TOXIC SUBSTANCESOPP OFFICIAL RECORD  
HEALTH EFFECTS DIVISION  
SCIENTIFIC DATA REVIEWS  
EPA SERIES 361MEMORANDUM**Date:** December 1, 2009**Subject:** **Flurprimidol:** Screening Assessment of Combined Exposure from Residential and Drinking Water Sources Based on Expansion of the Use Pattern to Include Application to Residential Turf.**PC Code:** 125701**DP Barcode:** D371753**MRID No.:** NA**Registration No.:** 67690-16, 67690-13,  
67690-15, 67690-19, 67690-44, and 67690-46**Petition No.:** NA**Regulatory Action:** Section 3 Registration**Assessment Type:****Reregistration Case No.:** NA

Screening level risk assessment

**TXR No.:** NA**CAS No.:** 56425-91-3**Decision No.:** 398756**40 CFR:** NA**To:** Rosemary Kearns/Tony Kish (RM22)  
Registration Division (7505P)  
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Risk Assessment Branch 2  
Health Effects Division (7509P)*R. Loranger*  
*for*Background

Flurprimidol is a turf grass and woody-plant growth regulator that belongs to the pyrimidine class of chemicals. Flurprimidol works through inhibition of gibberellin biosynthesis in the early stages of the pathway, which prevents normal plant growth and development. Currently registered formulations include water-soluble packets, liquid concentrate, granule and soluble concentrate. The percentage of active ingredient ranges from less than 1% (e.g., landscape, woody ornamental plants, and perennial ground covers) to 99.3% (e.g., ornamental trees). The

registered uses include applications to numerous sites: perennial turfgrass (cool and warm season) on golf courses and general turf, landscape/woody ornamental plants, trunk/ornamental trees and ornamental plants grown in containers in commercial nurseries, greenhouses and shadehouses. There are no existing or proposed food uses for flurprimidol.

HED recently evaluated the proposed expansion of the use pattern for 5 end-use products containing flurprimidol to include use on turf and ornamentals in residential and non-occupational settings; in addition, homeowner application was proposed for one of these products. HED evaluated occupational and residential exposure and risk associated with the proposed use expansion, and concluded there were no risks of concern for occupational handlers and those re-entering treated areas (occupational postapplication); furthermore, residential handler (adults) and postapplication risks (for both adults and children) were also not of concern [S. Wang, DP Barcode No. D357307, 10/12/09].

The 1996 Food Quality Protection Act (FQPA) requires HED/EPA to combine (aggregate) exposure and risk from food, drinking water and residential sources whenever food uses are assessed. Since there are no food uses for flurprimidol, HED is not required to conduct an aggregate risk assessment. However, since the use of flurprimidol on residential turf will result in potential dermal and incidental oral exposure to children, in addition to potential exposure through drinking water, HED has conducted a screening-level assessment of combined residential and drinking water exposures to ensure there are no potential risks to children, a vulnerable subpopulation, as a result of the use. In addition, upper-bound estimates of drinking water (dietary) exposure and risk have been provided for females 13-49 (acute) and the general US population (chronic). These exposure and risk estimates have been provided herein for risk management purposes.

### Screening Level Risk Scenarios

Based on the toxicity profile of flurprimidol, and on the potential exposure pathways associated with the use on turf, the following screening level risk scenarios have been assessed:

- 1) Acute dietary (drinking water), Females 13-49
- 2) Chronic dietary (drinking water), General US Population and all Population Subgroups
- 3) Short-term "aggregate" (drinking water + incidental oral + dermal), Children/Toddlers

For the purpose of this combined drinking water and residential exposure and risk assessment, acute and chronic dietary endpoints for risk assessment were selected from the submitted toxicology studies. Details regarding the studies selected, along with the associated NOAELs (no observed adverse effects levels) and the endpoints observed at the lowest observed adverse effect levels (LOAELs) are provided in Appendix 1. The endpoints selected for short-term dermal and oral risk assessment were described in detail in the 10/12/09 S. Wang risk assessment.

### Summary of Exposure to Children on Turf

As stated in the 10/12/09 S. Wang memo, postapplication dermal and incidental oral exposures

are not of concern for children/toddlers who come into contact with treated turf. In conjunction with the use on turf, children's postapplication exposure through dermal contact, incidental oral (hand-to-mouth) exposure, as well as object-to-mouth, soil ingestion, and incidental ingestion of granules were assessed. Details regarding the calculation of these exposures and risks were provided in the 10/12/09 S. Wang document. The lowest margin of exposure (MOE) was 190, for ingestion of granules, and all others were higher, indicating no risks of concern; the level of concern, or LOC, for all scenarios is an MOE of 100 or greater (i.e., MOEs less than 100 represent a risk concern).

HED typically combines dermal and incidental oral exposure with exposure from food and drinking water sources; the assumptions used in the dermal and incidental oral scenarios are considered to be high-end and conservative, and are therefore protective of other sources of exposure, such as soil ingestion and object-to-mouth. The ingestion of granules is considered to be episodic, and should not be combined with background exposure from food and drinking water. For the purpose of this screening assessment for flurprimidol, and in accordance with typical HED policy, only the dermal and incidental oral exposures have been combined with drinking water exposure. The summary of postapplication exposures to children/toddlers is presented in Table 1.

Applied Product	Application Rate (lb ai/A)	Postapplication Scenarios	Average Daily Dose (mg/kg/day)	MOE <sup>1</sup>
Cutless 50W	1.5 <sup>2</sup>	Dermal	0.0350	290
		Incidental Oral	0.0224	450

<sup>1</sup> MOE = Margin of Exposure, determined by dividing the NOAEL (no observed adverse effects level) by the average daily dose. For short-term dermal and incidental oral exposures, the NOAEL was 10 mg/kg/day, selected from a developmental rat study in which decreased body weight and food consumption were observed in the dams at the LOAEL (lowest observed adverse effects level) of 45 mg/kg/day.

<sup>2</sup> The single application rate of 1.5 lbs ai/A was used for assessing postapplication exposure on turf. Up to 2 applications are allowed per season at this rate.

Flurprimidol Estimated Drinking Water Concentrations (EDWCs)

A formal assessment describing drinking water model inputs and assumptions was not provided by the Environmental Fate and Effects Division (EFED). However, in a personal communication dated 7/24/09, Stephanie Syslo provided FIRST (FQPA Index Reservoir Screening Tool) modeled drinking water estimates for both peak (acute) and average (chronic) durations, with the direct output from the model shown below. These concentrations are based on the maximum seasonal application rate of 3 lbs ai/season.

Table 2. FIRST Modeled Estimated Drinking Water Concentrations for Flurprimidol.

UNTREATED WATER CONC (MICROGRAMS/LITER (PPB)) Ver 1.1.0 JAN 1, 2007

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PEAK DAY (ACUTE) CONCENTRATION	ANNUAL AVERAGE (CHRONIC) CONCENTRATION
244.311	73.333

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### Dietary Exposure from Drinking Water

The only potential source of dietary exposure to flurprimidol is through drinking water. The EDWCs shown in Table 2 were entered into the dietary exposure model. The model used was 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. To determine potential exposure to flurprimidol through drinking water, the acute value of 244 ppb (0.244 ppm) was used in the acute assessment, and the value of 73 ppb (0.073 ppm) was used for the chronic assessment. The input and output files for these assessments are provided in Appendix 2.

### Calculation of Screening Level Risks from Drinking Water and Residential Exposure

Both acute and chronic exposure from potential residues in drinking water are below HED's level of concern for dietary exposure. Details are provided in Appendix 2. At the 95<sup>th</sup> percentile of exposure, females 13-49 had an acute exposure of 0.011876 mg/kg/day, or 12% of the acute reference dose (aRfD). For chronic exposure, the highest exposed population subgroup was all infants, with an exposure of 0.005045 mg/kg/day, or 34% of the chronic reference dose (cRfD). Drinking water exposure was lower for all other subpopulations, including the general US population, for which exposure was 0.001539 mg/kg/day or 10% of the cRfD. HED is only concerned if exposures exceed 100% of the corresponding reference dose, and therefore acute and chronic exposure from flurprimidol residues in drinking water are not of concern.

### Screening-Level Combined Residential and Drinking Water Exposure

The residential postapplication dermal and incidental oral exposures from Table 1 were combined with the dietary exposure for all infants (i.e., the highest exposure for any children's subpopulation) to determine a screening-level "aggregate" exposure.

$$\begin{aligned} \text{Exposure} &= 0.0350 \text{ mg/kg/day}_{\text{dermal}} + 0.0224 \text{ mg/kg/day}_{\text{oral}} + 0.0050 \text{ mg/kg/day}_{\text{water}} \\ &= 0.0624 \text{ mg/kg/day} \end{aligned}$$

$$\text{MOE}_{\text{Combined}} = \text{NOAEL}/\text{Exposure} = 10/0.0624 \text{ mg/kg/day} = \mathbf{160}$$

Given that the combined MOE for drinking water and residential exposure is 160, HED has no concern for risks from any pathway or the combined pathways of exposure in conjunction with the proposed use expansion.

### Conclusions/Summary

HED is not strictly required to conduct an aggregate assessment for the non-food use expansion for flurprimidol. However, HED notes that when upper-bound assumptions regarding potential residues in drinking water are considered along with conservative estimates of residential exposure to children, the combined exposure and risk are not of concern. Furthermore, drinking water exposure is not of concern for any population subgroup.

## Appendix 1. Endpoint and Dose Selection for Fluprimidol Acute and Chronic Dietary Risk Assessment (L. Hansen, 8/4/2009)

### Acute Reference Dose (aRfD) – General Population

An appropriate endpoint was not identified for the general population because there were no relevant toxic effects observed in the submitted toxicology studies that could have resulted from a single dose.

### Acute Reference Dose (aRfD) - Females Age 13 to 49

**Study Selected:** Developmental Toxicity (rat)

**MRID No.:** 00147301

**Dose and Endpoint for Risk Assessment:** Developmental toxicity NOAEL = 10 mg/kg/day based on increased incidence of skeletal abnormalities, microphthalmia, hydronephrosis and hydronephrosis at the LOAEL = 45 mg/kg/day.

**Uncertainty Factor(s):** An UF of 100 was applied to account for inter-species extrapolation (10x) and intra-species variation (10x).

**Comments about Study/Endpoint/Uncertainty Factors:** The developmental toxicity NOAEL of 10 mg/kg/day represents the most sensitive endpoint available for this exposure scenario. The route of exposure (oral) is appropriate and the observed developmental effects potentially may result from a single exposure. The NOAEL is protective of developmental effects. An offspring NOAEL of 7.3 mg/kg/day was observed in the rat reproductive toxicity study (MRID 00162770), with a LOAEL of 74 mg/kg/day (decreased survival and pup body weights). The slightly lower NOAEL in the reproductive study is attributed to dose selection rather than greater sensitivity of the endpoint. A combined uncertainty factor (UF) of 100 (10x interspecies extrapolation and 10x intraspecies variability) was used. An additional database uncertainty factor (UF<sub>DB</sub>) due to lack of the neurotoxicity and immunotoxicity studies was not applied because there is no evidence of neurotoxicity or immunotoxicity in the available studies.

$$\text{Acute RfD} = \frac{10 \text{ mg/kg/day (NOAEL)}}{100 \text{ (UF)}} = 0.10 \text{ mg/kg/day}$$

### Chronic Reference Dose (cRfD) – All Populations

**Study Selected:** 90-Day Oral Toxicity (dog)

**MRID No.:** 00162768

**Dose and Endpoint for Risk Assessment:** NOAEL = 1.5 mg/kg/day based on adrenal effects (small size, decreased weight and histopathology) at LOAEL = 30 mg/kg/day.

**Uncertainty Factor(s):** An UF of 100 was applied to account for inter-species extrapolation (10X) and intra-species variation (10X).

**Comments about Study/Endpoint/Uncertainty Factors:** The NOAEL of 1.5 mg/kg/day represents the most sensitive oral endpoint available for this exposure scenario. The dog subchronic study was selected instead of a chronic study because both chronic studies had higher NOAELs (3.6 mg/kg/day in rat with a LOAEL of 12.1 mg/kg/day; and 7.0 mg/kg/day in dog with a LOAEL of 30 mg/kg/day). The selection of this endpoint from a subchronic duration study is

supported by the rat reproductive toxicity study parental NOAEL of 1.8 mg/kg/day, based on clinical signs of toxicity and liver histopathology at the LOAEL of 7.3 mg/kg/day (MRID 00162770). Furthermore, the endpoint is protective of developmental effects, which were observed only at higher doses (developmental/reproductive NOAELs  $\geq 7.3$  mg/kg/day). A combined uncertainty factor (UF) of 100 (10x interspecies extrapolation and 10x intraspecies variability) was used. An additional database uncertainty factor (UF<sub>DB</sub>) due to lack of neurotoxicity and immunotoxicity studies was not applied because there is no evidence of neurotoxicity or immunotoxicity in the available studies. An additional uncertainty factor for extrapolation of subchronic to chronic exposure (UF<sub>S</sub>) was not applied because the subchronic NOAEL was lower than the NOAELs from the chronic studies.

$$\text{Chronic RfD} = \frac{1.5 \text{ mg/kg/day (NOAEL)}}{100 \text{ (UF)}} = 0.015 \text{ mg/kg/day}$$

## Appendix 2. DEEM-FCID Model Inputs and Outputs for Acute/Chronic Dietary

### Acute DW Analysis – DEEM Input File

U.S. Environmental Protection Agency Ver. 2.02  
 DEEM-FCID Acute analysis for FLURPRIMIDOL  
 Residue file name: C:\Documents and Settings\cswart02.AA\My  
 Documents\RAB2chemicals\Flurprimidol\flurprimidol\_Screen\_acute.R98  
 Analysis Date 11-25-2009 Residue file dated: 11-16-2009/10:19:46/8  
 Reference dose: aRfD = 0.1 mg/kg bw/day NOEL = 10 mg/kg bw/day  
 Comment: RfDs, not PADS - screening level DW analysis

EPA Code	Crop Grp	Food Name	Def Res (ppm)	Adj. Factors #1	Adj. Factors #2	Comment
86010000	0	Water, direct, all sources	0.244000	1.000	1.000	
86020000	0	Water, indirect, all sources	0.244000	1.000	1.000	

### Acute DW Analysis – DEEM Output File

U.S. Environmental Protection Agency Ver. 2.02  
 DEEM-FCID ACUTE Analysis for FLURPRIMIDOL (1994-98 data)  
 Residue file: flurprimidol\_Screen\_acute.R98 Adjustment factor #2 NOT used.  
 Analysis Date: 11-25-2009/17:31:34 Residue file dated: 11-16-2009/10:19:46/8  
 NOEL (Acute) = 10.000000 mg/kg body-wt/day  
 Daily totals for food and foodform consumption used.  
 Run Comment: "RfDs, not PADS - screening level DW analysis"

Summary calculations (per capita):

95th Percentile			99th Percentile			99.9th Percentile		
Exposure	% aRfD	MOE	Exposure	% aRfD	MOE	Exposure	% aRfD	MOE
<b>Females 13-49 yrs:</b>								
0.011876	11.88	842	0.019114	19.11	523	0.033897	33.90	295

### Chronic DW Analysis – DEEM Input File

U.S. Environmental Protection Agency Ver. 2.00  
 DEEM-FCID Chronic analysis for FLURPRIMIDOL 1994-98 data  
 Residue file: C:\Documents and Settings\cswart02.AA\My  
 Documents\RAB2chemicals\Flurprimidol\flurprimidol\_Screen\_chronic.R98  
Adjust. #2 NOT used  
 Analysis Date 11-25-2009 Residue file dated: 11-16-2009/10:20:06/8  
 Reference dose (RfD) = 0.015 mg/kg bw/day  
 Comment: RfDs, not PADS - screening level DW analysis

Food EPA Code	Crop Grp	Food Name	Residue (ppm)	Adj. Factors #1	Adj. Factors #2	Comment
86010000	0	Water, direct, all sources	0.073000	1.000	1.000	
86020000	0	Water, indirect, all sources	0.073000	1.000	1.000	

**Chronic DW Analysis - DEEM Output File**

U.S. Environmental Protection Agency Ver. 2.00  
 DEEM-FCID Chronic analysis for FLURPRIMIDOL (1994-98 data)  
 Residue file name: C:\Documents and Settings\cswart02.AA\My  
 Documents\RAB2chemicals\Flurprimidol\flurprimidol\_screen\_chronic.R98  
 Adjustment factor #2 NOT used.  
 Analysis Date 11-25-2009/17:32:38 Residue file dated: 11-16-2009/10:20:06/8  
 Reference dose (RfD, Chronic) = .015 mg/kg bw/day  
 COMMENT 1: RfDs, not PADs - screening level DW analysis

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Total exposure by population subgroup

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Population Subgroup	Total Exposure	
	mg/kg body wt/day	Percent of Rfd
U.S. Population (total)	0.001539	10.3%
U.S. Population (spring season)	0.001525	10.2%
U.S. Population (summer season)	0.001653	11.0%
U.S. Population (autumn season)	0.001487	9.9%
U.S. Population (winter season)	0.001488	9.9%
Northeast region	0.001404	9.4%
Midwest region	0.001556	10.4%
Southern region	0.001463	9.8%
Western region	0.001763	11.8%
Hispanics	0.001747	11.6%
Non-hispanic whites	0.001501	10.0%
Non-hispanic blacks	0.001461	9.7%
Non-hisp/non-white/non-black	0.001886	12.6%
All infants (< 1 year)	0.005045	33.6%
Nursing infants	0.001871	12.5%
Non-nursing infants	0.006249	41.7%
Children 1-6 yrs	0.002150	14.3%
Children 7-12 yrs	0.001398	9.3%
Females 13-19 (not preg or nursing)	0.001083	7.2%
Females 20+ (not preg or nursing)	0.001536	10.2%
Females 13-50 yrs	0.001489	9.9%
Females 13+ (preg/not nursing)	0.001496	10.0%
Females 13+ (nursing)	0.002132	14.2%
Males 13-19 yrs	0.001132	7.5%
Males 20+ yrs	0.001379	9.2%
Seniors 55+	0.001511	10.1%
Children 1-2 yrs	0.002285	15.2%
Children 3-5 yrs	0.002139	14.3%
Children 6-12 yrs	0.001475	9.8%
Youth 13-19 yrs	0.001112	7.4%
Adults 20-49 yrs	0.001437	9.6%
Adults 50+ yrs	0.001511	10.1%
Females 13-49 yrs	0.001431	9.5%

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# R179477

**Chemical Name:** Flurprimidol

**PC Code:** 125701

**HED File Code:** 12000 Exposure Reviews

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12/10/2009