



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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

MEMORANDUM

DATE: May 1, 2003

SUBJECT: **Benfluralin.** Chronic Dietary Exposure Assessment for the Reregistration Eligibility Decision (RED).

PC Code: 084301
DP Barcode: D267994

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TO: Rich Griffin, Biologist
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Executive Summary

The purpose of this memorandum is to report the results of a dietary exposure analysis for benfluralin. In this analysis the chronic dietary exposure and risk estimates resulting from food intake were determined for the general U.S. population and various population subgroups. The analysis was performed to support the reregistration eligibility decision (RED).

The conservative Tier1 chronic dietary exposure assessment was conducted for all supported benfluralin food uses. Dietary risk estimates are provided for the general U.S. population and various population subgroups. This assessment concludes that for all supported commodities, the chronic dietary exposure estimates are below HED's level of concern (<100% cPAD¹) for the general U.S. population (<1% of the cPAD) and all population subgroups. The chronic dietary exposure estimate for the highest exposed population subgroup, adults 20-49 years of age is <1% of the cPAD.

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. HED is generally concerned when estimated cancer risk exceeds one in one million (i.e., the risk exceeds 1×10^{-6}). 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).

II. Residue Information

Benfluralin (also known as benefin; N-butyl-N-ethyl- " , " , " -trifluoro-2,6-dinitro-p-toluidine) is an herbicide registered for use on alfalfa, birdsfoot trefoil, clover, and lettuce. Tolerances are established under 40 CFR §180.208 and are currently expressed in terms of negligible residues of the herbicide benfluralin *per se* in/on the raw agricultural commodities (RACs). No benfluralin tolerances have been established for animal [Category 3, 40 CFR §180.6(a)] or processed food/feed commodities and there are no SLN registrations for use of benfluralin on food/feed crops. Adequate methods are available for the purpose of tolerance enforcement. The Pesticide Analytical Manual (PAM, Vol. II, Section 180.208) lists two methods (designated as Methods I and A) as available for determination of benfluralin *per se* in/on plant commodities.

The reregistration of benfluralin is being supported by Dow AgroSciences LLC (formerly DowElanco) and Platte Chemical Company; only Platte Chemical Company currently holds an active benfluralin registration with food/feed uses. Benfluralin products are sold under the trade name Balan™ and may

¹ cPAD = acute/chronic Population Adjusted Dose = $\frac{\text{Acute or Chronic RfD}}{\text{FQPA Safety Factor}}$

be applied as preplant soil incorporated treatments to alfalfa, birdsfoot trefoil, clover, and lettuce using ground equipment. Benfluralin end-use products with registered food/feed uses are formulated as dry flowable formulations (DFs).

On March 19, 2003, the Metabolism Assessment Review Committee met to discuss benfluralin residues of concern in plants, livestock, and drinking water. The MARC reaffirmed that benfluralin *per se* is the residue of concern for tolerance expression and for dietary risk assessment. Tolerances for residues of benfluralin in or on plant commodities are currently expressed in terms of negligible residues of the herbicide N-butyl-N-ethyl-4-chloro-2,6-dinitro-p-toluidine in or on the raw agricultural commodities.

Table 1. Tolerance Values Used in Chronic Benfluralin Dietary Exposure Analysis			
RAC	Classification ¹	Data Source ²	Reassessed Tolerance
Lettuce	NB	MRID: 43831902	0.05

1. Classification of blended (B), partially blended (PB), not blended (NB).

III. DEEM-FCID™ Program and Consumption Information

The benfluralin chronic dietary exposure assessment was conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™, Version 1.3) 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. Consumption data are averaged for the entire U.S. population and within population subgroups for chronic exposure assessment, but are retained as individual consumption events for acute exposure assessment. 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 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 exposure and risk 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. The resulting residue consumption estimate for each food/food form is summed with the residue consumption 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.

IV. Toxicological Information

On January 11, 2001, the Health Effects Division (HED) Hazard Identification Assessment Review Committee (HIARC) reviewed the recommendations of the toxicology reviewer for benfluralin with regard to the acute and chronic Reference Doses (RfDs) and the toxicological endpoint selection for use as appropriate in occupational/residential exposure risk assessments. On December 17, 2002, the HED HIARC met to: (1) revise the FQPA assessment according to the OPP 10x Guidance document of 2002, and (2) re-evaluated the acute RfD.

The toxicity data base is adequate for FQPA consideration. The HIARC concluded that the FQPA Safety factor should be removed because there is no susceptibility and no residual uncertainty.

Table 2. Summary of Toxicological Doses and Endpoints for Benfluralin for Use in Dietary Exposure Assessment			
Exposure Scenario	Dose used in Risk Assessment, UF (mg/kg/day)	Special FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary	An appropriate endpoint attributable to a single dose was not identified. Therefore, an acute RfD was not established		
Chronic Dietary (All populations)	NOAEL = 0.5 mg/kg/day UF = 100 Chronic RfD = 0.005 mg/kg/day	*FQPA SF = 1X cPAD = 0.005/1 = 0.005 mg/kg/day	Chronic /carcinogenicity-Rat LOAEL = 5.4 based on increased histopathologic lesions of the kidneys were seen in males (5.4 mg/kg/day and females 6.8 mg/kg/day for females).

According to the Agency’s Draft Guidelines for Cancer Risk Assessment (July, 1999), the CARC classified benfluralin into the category **“Suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential”** based on the occurrence of liver tumors in female mice. “The Committee further recommended that the quantification of human cancer risk is not required.”

Contributing factors to the CARC (TXR# 0050378) decision were, (1) the lack of carcinogenic potential in rats, (2) a lack of mutagenic potential in a battery of tests, (3) structurally related pesticides such as trifluralin, ethalfuralin, oryzalin, flumetralin and pendimethalin were classified as “C” carcinogens and their respective mutagenicity studies showed no uniform pattern of mutagenicity.

V. Results/Discussion

As stated above, for 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 Tables 3 and 4 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.

Results of Chronic Dietary Exposure Analysis

Table 3. Results of Chronic Benfluralin Dietary Exposure Analysis			
Population Subgroup	cPAD (mg/kg/day)	Exposure (mg/kg/day)	% cPAD
General U.S. Population	0.005	0.000012	<1
All Infants (< 1 year old)	0.005	0.000000	0
Children 1-2 years old	0.005	0.000007	<1
Children 3-5 years old	0.005	0.000010	<1
Children 6-12 years old	0.005	0.000011	<1
Youth 13-19 years old	0.005	0.000011	<1
Adults 20-49 years old	0.005	0.000014	<1
Females 13-49 years old	0.005	0.000012	<1
Adults 50+ years old	0.005	0.000014	<1

VI. Discussion of Uncertainties

The conservative Tier 1 dietary exposure assessment for benfluralin could be refined for more realistic dietary exposure estimates using percent crop treated and market share estimates, field trial and monitoring data, and processing data; however, the estimated dietary risk to benfluralin is not of concern for all populations in chronic dietary exposure assessments and do not require refinements at this time.

VII. Conclusions

The conservative Tier1 chronic dietary exposure assessment was conducted for all supported benfluralin food uses. This assessment concludes that for all supported commodities, the chronic dietary exposure estimates are below HED's level of concern (<100% cPAD) for the general U.S. population (<1% of the cPAD) and all population subgroups. Further refinement to this dietary exposure assessment is not required at this time.

Table 4. Summary of Dietary Exposure and Risk for Benfluralin			
Population Subgroup**	Chronic Dietary		Cancer
	Dietary Exposure (mg/kg/day)	% cPAD	Risk
General U.S. Population	0.000012	<1	Not Applicable
All Infants (< 1 year old)	0.000000	0	N/A
Children 1-2 years old	0.000007	<1	
Children 3-5 years old	0.000010	<1	
Children 6-12 years old	0.000011	<1	
Youth 13-19 years old	0.000011	<1	
*Adults 20-49 years old	0.000014	<1	
Females 13-49 years old	0.000012	<1	
*Adults 50+ years old	0.000014	<1	

* The values for the highest exposed population for each type of risk assessment should be bolded.

VIII. List of Attachments

- Attachment 1: Chronic Residue Input File
- Attachment 2: Chronic Results

cc: Sherrie L. Kinard (RRB2), Bill Cutchin. RD/I: Benfluralin Team Review (4/2/03), Dietary Exposure SAC (4/17/03), A. Nielsen (5/1/03).

7509C: RRB2: S. Kinard: CM#2:Rm 722B: 703-305-0563: 5/1/03.

Attachment 1

U.S. Environmental Protection Agency Ver. 1.30
DEEM-FCID Chronic analysis for BENFLURALIN 1994-98 data
Residue file: C:\MyFiles\Benfluralin\Benfluralin.R98 Adjust. #2 NOT used
Analysis Date 04-02-2003 Residue file dated: 04-01-2003/13:59:52/8
Reference dose (RfD) = 0.005 mg/kg bw/day

Food Crop			Residue	Adj.Factors		Comment
EPA Code	Grp	Food Name	(ppm)	#1	#2	
04012040	4A	Lettuce, head	0.050000	1.000	1.000	
04012050	4A	Lettuce, leaf	0.050000	1.000	1.000	

Attachment 2

U.S. Environmental Protection Agency Ver. 1.30
DEEM-FCID Chronic analysis for BENFLURALIN (1994-98 data)
Residue file name: C:\MyFiles\Benfluralin\Benfluralin.R98
Adjustment factor #2 NOT used.
Analysis Date 04-01-2003/14:00:39 Residue file dated: 04-01-2003/13:59:52/8
Reference dose (RfD, Chronic) = .005 mg/kg bw/day

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Total exposure by population subgroup

Population Subgroup	Total Exposure	
	mg/kg body wt/day	Percent of Rfd
U.S. Population (total)	0.000012	0.2%
U.S. Population (spring season)	0.000013	0.3%
U.S. Population (summer season)	0.000012	0.2%
U.S. Population (autumn season)	0.000012	0.2%
U.S. Population (winter season)	0.000012	0.2%
Northeast region	0.000012	0.2%
Midwest region	0.000013	0.3%
Southern region	0.000010	0.2%
Western region	0.000014	0.3%
Hispanics	0.000012	0.2%
Non-hispanic whites	0.000013	0.3%
Non-hispanic blacks	0.000007	0.1%
Non-hisp/non-white/non-black	0.000013	0.3%
All infants (< 1 year)	0.000000	0.0%
Nursing infants	0.000000	0.0%
Non-nursing infants	0.000000	0.0%
Children 1-6 yrs	0.000009	0.2%
Children 7-12 yrs	0.000011	0.2%
Females 13-19 (not preg or nursing)	0.000011	0.2%
Females 20+ (not preg or nursing)	0.000014	0.3%
Females 13-50 yrs	0.000014	0.3%
Females 13+ (preg/not nursing)	0.000013	0.3%
Females 13+ (nursing)	0.000015	0.3%
Males 13-19 yrs	0.000011	0.2%
Males 20+ yrs	0.000012	0.2%
Seniors 55+	0.000011	0.2%
Children 1-2 yrs	0.000007	0.1%
Children 3-5 yrs	0.000010	0.2%
Children 6-12 yrs	0.000011	0.2%
Youth 13-19 yrs	0.000011	0.2%
Adults 20-49 yrs	0.000014	0.3%
Adults 50+ yrs	0.000012	0.2%
Females 13-49 yrs	0.000014	0.3%
