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

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

February 18, 1999

MEMORANDUM

SUBJECT: **Terbufos.** List A Reregistration Case No. 0109/Chemical ID No. 105001.
Revised Probabilistic (Monte Carlo) Acute Dietary Exposure and Risk. No
MRID #. DP Barcode No. D253373.

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Christina Swartz

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TO: William J. Hazel, Ph.D.
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and

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Special Review Branch
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Background

In conjunction with the preparation of a revised risk assessment for the active ingredient terbufos, HED conducted an in-house probabilistic (Monte Carlo) acute dietary exposure and risk analysis using residue distribution files (RDFs) provided by American Cyanamid (AMCY) which were modified in accordance with HED's policy for estimation of acute dietary exposure for blended commodities (refer to the C. Swartz memo dated 1/20/99, DP Barcode Nos. D249385 and D250807). The estimated acute dietary exposure and risk exceeded the Agency's level of concern for the general US population and additional population subgroups including infants and children.

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Present Considerations

Previous acute dietary risk assessments were conducted using an acute endpoint and reference dose selected from a 28-day oral dog study. Based on the recent selection of an endpoint and dose (No Observable Adverse Effects Level, NOAEL) from an acute oral neurotoxicity study in the rat, HED has conducted a revised probabilistic acute dietary exposure and risk assessment. The previously conducted chronic dietary exposure assessment, which indicated that chronic dietary exposure and risk for terbufos are below the Agency's level of concern, need not be revised.

Additional acute dietary exposure analyses were conducted in which selected commodities were excluded from the analysis. The purpose of the additional work was to provide better characterization for risk mitigation options for terbufos.

SUMMARY

The revised analysis indicates that acute dietary exposure and risk estimates for terbufos exceed the Agency's level of concern for population subgroups including infants and children. When all commodities are included in the analysis, the percent of the acute population adjusted dose (PAD, the acute reference dose divided by the FQPA Safety Factor), or %aPAD, consumed for the general US population is below the Agency's level of concern, at approximately 68 %aPAD. The most highly exposed population subgroup is non-nursing infants (<1 year), at approximately 260 % aPAD.

The analyses in which selected commodities were excluded confirm that bananas are the most significant contributor to acute dietary exposure to terbufos. Exclusion of field corn or sweet corn from the analysis resulted in virtually no change in the %aPAD consumed (at the 99.9th percentile of exposure) for the most highly exposed subgroups. However, exclusion of bananas from the assessment resulted in acute dietary risk significantly below the Agency's level of concern, with at most 50% aPAD consumed (children 1-6).

DETAILED CONSIDERATIONS

Hazard Information

Previous acute dietary risk assessments were conducted using an acute NOAEL selected from a 28-day oral dog study, in which cholinesterase inhibition was observed on day 7 at the LOAEL of 0.015 mg/kg/day. In an attempt to select an appropriate time-related endpoint for acute dietary risk assessment, the HED Hazard Identification Assessment Review Committee (HIARC) re-examined the rat and dog studies to determine a species sensitivity factor to be applied to the endpoint and NOAEL selected from the oral acute neurotoxicity study in the rat. The endpoint and dose selected from the rat study, combined with the relevant uncertainty factors and the species sensitivity factor, should be used in HED acute dietary risk assessments.

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The revised probabilistic acute dietary exposure and risk analysis has been conducted using the revised acute NOAEL of 0.15 mg/kg/day; the combined uncertainty factors of 1500X include 10X for inter-species extrapolation, 10X for intra-species variability, a 5X species sensitivity factor, and an additional 3X as required by FQPA. The revised acute population adjusted dose (aPAD), which is the acute reference dose with the FQPA safety factor applied, is 0.0001 mg/kg/day.

Consumption Data

The HED acute dietary probabilistic exposure assessment was conducted using the Dietary Exposure Evaluation Model (DEEM™) software, which uses single-day consumption data generated in USDA's Continuing Survey of Food Intake by Individuals (CSFII, 1989-1991) and anticipated residues in relevant commodities as described below.

Usage/Percent Crop Treated (%CT) Information

A quantitative usage analysis (QUA) was completed by BEAD/OPP (Dhol Herzi memo dated 10/98). The registrant's %CT estimates were generally similar to those provided by BEAD/OPP. To further refine the dietary risk assessments for terbufos, both AMCY and BEAD estimated the %CT for bananas using Landell Mills; Agency and AMCY estimates for bananas were also comparable. The data were summarized in the 1/20/99 C. Swartz memo, and are included in Table 1 (see below).

Residue Information

No new residue information have been generated for the revised acute dietary risk assessment. The summary of RDFs used in the previous assessment, as well as anticipated residues (ARs) for blended commodities, are shown in Table 1; the RDFs for bananas and sweet corn are included in Appendix 1.

Table 1. Summary of Terbufos Residue Distribution Files (AMCY) and Anticipated Residues for Blended Commodities.¹

Commodity	MRID Nos.	1X Rate	AMCY %CT	# Residue Values Used in RDF	# Zeros	Total # of Values in RDF
Bananas	262634 44629302	3 g ai/mat	27.7	14 (x 250) ² = 3,500	9,231	12,771
		4 g ai/mat	0.3	40 (x 1) = 40		
Field Corn	44629303, 41955604, 00036238, 00035963, 00035962, 232258, 091452 GS0109001	1.3 lb ai/A	8	AR = 0.00024 [Average residue of 0.003 ppm x 8%CT]	NA	NA
Sweet Corn	43237802	1.3 lb ai/A	8	14	167	181
Sugar Beets	42267901, 41569401, 0036214	4.35 lb ai/A	37	NA	NA	NA
Grain Sorghum	42661801, 41569402	3.92	4	NA	NA	NA
Coffee	40365901	1 g ai/plant	1	AR = 0.00028 ppm ³ [Average residue of 0.028 ppm x 1%CT]	NA	NA

- ¹ Shaded areas of the table indicate blended commodities for which anticipated residues were calculated (a point estimate was used, rather than an RDF). Note that sugar beets were not included in the analysis, since terbufos is degraded during processing into sugar. No consumption events were identified for grain sorghum, in the 1989-1991 CSFII; therefore, grain sorghum was excluded from the analysis.
- ² The following approach was used by AMCY to generate the banana RDF: In order to account for the percentage of imported bananas treated at the 2 different 1X rates, residue values for bananas treated at the lower rate were weighted by counting each value 250 times in the residue distribution file. The residue values from the higher rate field trials were each counted once.
- ³ HED does not consider coffee to be a blended commodity; however, due to the relatively insignificant contribution of residues in coffee to dietary risk, HED has treated coffee as a blended commodity in this analysis.

Results

Results of the probabilistic acute dietary exposure and risk assessments are shown in Tables 2

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and 3. Table 2 shows the 95th, 99th and 99.9th percentile of exposure (and associated %aPAD consumed) for the general US population and various population subgroups when all commodities are included in the assessment. Table 3 shows the 99.9th percentile of exposure (and associated %aPAD consumed) when bananas, sweet corn, and field corn are alternately excluded from the analysis. Previous analyses in which coffee was excluded indicated that there was virtually no change in the risk when coffee was not considered; therefore, coffee was included in all the current assessments.

Table 2. Terbufos Revised Acute Dietary Exposure/Risk Estimates for Terbufos (All Commodities Included).¹

Population Subgroup	95th Percentile		99th Percentile		99.9th Percentile	
	Exposure	%aPAD	Exposure	%aPAD	Exposure	%aPAD
General US Population	0.000001	0.84	0.000018	17.9	0.000068	68.4
All infants (<1 yr)	0.000012	11.7	0.000087	86.6	0.000255	255
Nursing infants (<1 yr)	0.000000	0.08	0.000046	45.6	0.000131	131
Non-nursing infants	0.000016	16.0	0.000100	99.6	0.000261	261
Children (1-6 years)	0.000005	5.04	0.000048	47.6	0.000141	141
Children (7-12 years)	0.000001	0.62	0.000023	22.6	0.000068	67.8
Females (13-50 years)	0.000000	0.11	0.000012	11.6	0.000035	35.3
Males (20+ years)	0.000000	0.39	0.000011	10.9	0.000031	30.6

¹ Exposures are expressed as mg/kg body weight/day. aPAD = acute Population Adjusted Dose, (aRfD/FQPA safety factor).

Table 3. Summary of Terbufos Acute Dietary Exposure/Risk Estimates, Excluding Selected Commodities.¹

Results based on the 99.9th percentile

Population Subgroup	Excluding Bananas		Excluding Field Corn		Excluding Sweet Corn	
	Exposure	%aPAD	Exposure	%aPAD	Exposure	%aPAD
General US	0.000021	21.3	0.000072	71.7	0.000063	63.2
All infants	0.000010	9.68	0.000256	256	0.000246	246
Infants, nursing	0.000001	0.94	0.000125	125	0.000131	130
Infants, n-nursing	0.000014	13.8	0.000263	263	0.000261	261
Children (1-6)	0.000049	48.7	0.000144	144	0.000132	132
Children (7-12)	0.000033	32.6	0.000070	70.2	0.000062	61.6
Females (13-50)	0.000015	15.5	0.000038	37.8	0.000033	33.2
Males (20+ years)	0.000015	14.8	0.000034	34.2	0.000027	27.4

¹ Exposures are expressed as mg/kg body weight/day. aPAD = acute Population Adjusted Dose, (aRfD/FQPA safety factor).

The results of the analyses indicate that acute dietary exposure and risk estimates for terbufos exceed the Agency's level of concern for population subgroups including infants and children, even though the higher acute NOAEL selected from the rat study was used in the assessment. When all commodities are included in the analysis, the %aPAD consumed for the general US population is below the Agency's level of concern, at approximately 68 %aPAD. The most highly exposed population subgroup is non-nursing infants, at approximately 260 % aPAD.

The analyses in which selected commodities were excluded confirm that bananas are the most significant contributor to acute dietary exposure and risk for terbufos. Exclusion of field corn or sweet corn from the analysis resulted in virtually no change in the %aPAD consumed (at the 99.9th percentile of exposure) for the most highly exposed subgroups. However, exclusion of bananas from the assessment resulted in acute dietary risk significantly below the Agency's level of concern, with at most 50% aPAD consumed (children 1-6).

The results of the 4 analyses are attached as follows:

- Appendix 1: AMCY Residue Distribution Files (RDFs) for Bananas and Sweet Corn.
- Appendix 2: HED Revised Probabilistic Acute Dietary Risk Analysis/Rat NOAEL.
- Appendix 3: HED Probabilistic Acute Dietary Risk Analysis, Excluding Certain Commodities.

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cc: Reviewer, C. Swartz; List A File, DRES Files (M. Sahafeyen, HED/7509C)
CSwartz:RRB1:CM2:Rm 722:703 305 5877:2/18/99
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Appendix 1: AMCY Residue Distribution Files (RDFs) for Bananas and Sweet Corn.

Bananas

Nonnormalized field trials - bananas (half lod/loq)
adj for 3 g ai and 4 g ai rates
totalz=9231

250,0.016	1,0.00022	1,0.00023
250,0.01	1,0.00028	1,0.00024
250,0.005	1,0.0002	1,0.00062
250,0.005	1,0.0001	1,0.0008
250,0.015	1,0.0001	1,0.00061
250,0.005	1,0.0001	1,0.00051
250,0.005	1,0.00041	1,0.0001
250,0.005	1,0.00044	1,0.0001
250,0.005	1,0.00034	1,0.0001
250,0.005	1,0.00052	1,0.0001
250,0.005	1,0.00024	1,0.0001
250,0.005	1,0.00023	1,0.0001
250,0.005	1,0.00019	1,0.0002
250,0.005	1,0.00022	1,0.0001
1,0.005	1,0.0001	1,0.00047
1,0.005	1,0.00022	1,0.00041
1,0.005	1,0.0001	1,0.00039
1,0.011	1,0.0001	1,0.00037

Sweet Corn

CORN, SWEET 8% CT (LODs 1X applic only)
Totalz = 167
Totalnz = 14

0.0045	0.005	0.0025
0.005	0.01	0.002
0.005	0.005	0.0025
0.004	0.025	0.0025
0.0035	0.0025	

Appendix 2. Revised HED Probabilistic Acute Dietary Risk Analysis for Terbufos.

U.S. Environmental Protection Agency
 DEEM ACUTE analysis for TERBUFOS
 Residue file name: 105001c.R91
 Analysis Date: 02-11-1999/04:46:56
 Acute Reference Dose (aRfD) = 0.000100 mg/kg body-wt/day
 MC iterations = 1000
 Run Comment: using MC data files from AmCy; Acute NOAEL from rat; UFs total 15
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Ver. 6.27
 (1989-92 data)
 Adjustment factor #2 NOT used.
 Residue file dated: 02-11-1999/04:08:47/8
 MC list in residue file
 MC seed = 1026

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Summary calculations:

	95th Percentile		99th Percentile		99.9 Percentile	
	Exposure	% aRfD	Exposure	% aRfD	Exposure	% aRfD
U.S. pop - all seasons:	0.000001	0.84	0.000018	17.87	0.000068	68.39
All infants (<1 year):	0.000012	11.69	0.000087	86.62	0.000255	255.16
Nursing infants (<1 year):	0.000000	0.08	0.000046	45.65	0.000131	131.33
Non-nursing infants (<1 yr):	0.000016	16.00	0.000100	99.55	0.000261	261.20
Children (1-6 years):	0.000005	5.04	0.000048	47.61	0.000141	141.10
Children (7-12 years):	0.000001	0.62	0.000023	22.64	0.000068	67.77
Females (13-50 years):	0.000000	0.11	0.000012	11.60	0.000035	35.34
Males (20+ years):	0.000000	0.39	0.000011	10.88	0.000031	30.55

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Appendix 3: HED Revised Probabilistic Acute Dietary Risk Analysis Excluding Certain Commodities.

U.S. Environmental Protection Agency Ver. 6.27
 DEEM ACUTE analysis for TERBUFOS (1989-92 data)
 Residue file name: 105001m.R91 Adjustment factor #2 NOT used.
 Analysis Date: 02-11-1999/05:37:21 Residue file dated: 02-11-1999/04:59:23/8
 Acute Reference Dose (aRfD) = 0.000100 mg/kg body-wt/day
 MC iterations = 1000 MC list in residue file MC seed = 1026
 Run Comment: using MC data files from AmCy; Acute NOAEL from rat;
Assessment excludes bananas

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Summary calculations:

	95th Percentile		99th Percentile		99.9 Percentile	
	Exposure	% aRfD	Exposure	% aRfD	Exposure	% aRfD
U.S. pop - all seasons:	0.000001	1.02	0.000002	2.44	0.000021	21.31
All infants (<1 year):	0.000002	1.94	0.000003	2.86	0.000010	9.68
Nursing infants (<1 year):	0.000001	0.64	0.000001	0.89	0.000001	0.94
Non-nursing infants (<1 yr):	0.000002	2.08	0.000003	3.30	0.000014	13.79
Children (1-6 years):	0.000002	1.94	0.000005	5.43	0.000049	48.71
Children (7-12 years):	0.000001	1.41	0.000004	4.06	0.000033	32.56
Females (13-50 years):	0.000001	0.68	0.000001	1.22	0.000015	15.50
Males (20+ years):	0.000001	0.65	0.000001	1.32	0.000015	14.76

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Appendix 3: HED Revised Probabilistic Acute Dietary Risk Analysis Excluding Certain Commodities.

U.S. Environmental Protection Agency
 DEEM ACUTE analysis for TERBUFOS
 Residue file name: 105001fc.R91
 Analysis Date: 02-11-1999/06:00:44
 Acute Reference Dose (aRfD) = 0.000100 mg/kg body-wt/day
 MC iterations = 1000
 Run Comment: using MC data files from AmCy; acute NOAEL from rat;
Assessment excludes field corn

Ver. 6.27
 (1989-92 data)
 Adjustment factor #2 NOT used.
 Residue file dated: 02-11-1999/05:43:23/8
 MC list in residue file
 MC seed = 1026

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Summary calculations:

	95th Percentile		99th Percentile		99.9 Percentile	
	Exposure	% aRfD	Exposure	% aRfD	Exposure	% aRfD
U.S. pop - all seasons:	0.000002	1.61	0.000019	19.31	0.000072	71.71
All infants (<1 year):	0.000009	8.71	0.000084	83.66	0.000256	256.35
Nursing infants (<1 year):	0.000000	0.00	0.000041	40.69	0.000125	124.61
Non-nursing infants (<1 yr):	0.000016	16.26	0.000086	86.27	0.000263	262.64
Children (1-6 years):	0.000009	8.68	0.000050	49.70	0.000144	144.08
Children (7-12 years):	0.000003	2.64	0.000024	24.27	0.000070	70.22
Females (13-50 years):	0.000001	0.57	0.000014	13.56	0.000038	37.80
Males (20+ years):	0.000002	2.34	0.000013	12.68	0.000034	34.22

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Appendix 3: HED Revised Probabilistic Acute Dietary Risk Analysis Excluding Certain Commodities.

U.S. Environmental Protection Agency Ver. 6.27
 DEEM ACUTE analysis for TERBUFOS (1989-92 data)
 Residue file name: 105001sc.R91 Adjustment factor #2 NOT used.
 Analysis Date: 02-11-1999/20:14:18 Residue file dated: 02-11-1999/19:35:35/8
 Acute Reference Dose (aRfD) = 0.000100 mg/kg body-wt/day
 MC iterations = 1000 MC list in residue file MC seed = 1026
 Run Comment: using MC data files from AmCy; NOAEL from rat study; NOAEL from r
 at, combined UF of 1500;
Assessment excludes sweet corn
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Summary calculations:

	95th Percentile		99th Percentile		99.9 Percentile	
	Exposure	% aRfD	Exposure	% aRfD	Exposure	% aRfD
U.S. pop - all seasons:	0.000000	0.22	0.000016	15.97	0.000063	63.17
All infants (<1 year):	0.000012	11.52	0.000084	84.18	0.000246	246.18
Nursing infants (<1 year):	0.000000	0.08	0.000045	45.26	0.000131	130.54
Non-nursing infants (<1 yr):	0.000016	15.99	0.000087	86.85	0.000261	261.27
Children (1-6 years):	0.000001	1.18	0.000045	45.19	0.000132	132.21
Children (7-12 years):	0.000000	0.20	0.000020	20.36	0.000062	61.62
Females (13-50 years):	0.000000	0.09	0.000011	10.75	0.000033	33.22
Males (20+ years):	0.000000	0.10	0.000010	9.54	0.000027	27.42

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