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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM DEC 30

TO: Bruce Kapner, Product Manager
Special Pesticide Review Division (TS-791C)

THRU: Charles Frick, Acting Section Head
Review Section #5
Toxicology Branch/HED (TS-769)
and
Robert B. Jaeger, Acting Chief 12/30/82 for OEP
Toxicology Branch/HED (TS-769)

SUBJECT: Terbufos Registration Standard

Enclosed you will find the completed Toxicology Chapter for Terbufos Registration Standard and the completed reviews of the relevant toxicology studies for this chemical and its only formulation Counter 15G.

Amal Mahfouz 12/29/82
c. Frick for JC. 12/29/82

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Toxicology Branch
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cc: J. Heckman
T. Roetzel
R. Coberly (as per Bill Burnam memo of 3/17/83, received 3/2
3/22/8

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Toxicology

Chapter

All studies on Terbufos (Counter) have been sponsored by American Cyanamid, the major producer of Terbufos technical and Counter 15G formulation. Only three acute studies(*) have been sponsored by Aceto Chemical Company on their product, Enlist (86% a.i.). Summary and discussions of these data are presented on the following pages.

*See the following table.

Data Summary

CHEMICAL: Terbufos

CASWELL: 131A

Study/Lab/Study #/Date	MRID	Material	Accession Number	Results	Tox. Cat.	Core Classification
Acute Testing:						
Acute Oral LD50 - Rat American Cyanamid #A-72-95 12/5/72	00037467	85.8% in corn oil	112227	LD50 (M) = 1.6 (1.2-1.9) mg/kg (only one sex was tested)	I	Minimum
Acute Oral LD50 - Rat IBT#A1373 4/9/72	00037471	96.7% in corn oil	not reported	LD50 (F) = 1.3 + 0.2 mg/kg All animals exhibited signs of acute ChE inhibition. At necropsy, animals that died had gastrointestinal hemorrhage. (only one sex was tested)	I	Minimum
*Acute Oral LD50 - Rat Cannon Labs #6E-3164 11/9/76	00035121	86% in corn oil	not reported	LD50 (F) = 1.57 (1.15-2.15) mg/kg LD50 (M) = 1.74 (1.29-2.35) mg/kg LD50 (F&M) = 1.65 (1.35-2.03) mg/kg respiratory, depression, piloerection, clonic convulsions, exophthalmus, ptosis, lacrimation, hemorrhaging, decreased motor activity	I	Minimum

Study/Lab/Study #/Date	MRID	Material	Accession Number	Results	Tox. Cat.	Core Classification
*Acute Oral LD50 - Rat Consultox Labs #CL75:37:1131 4/75	00029863	86% in DMSO	not reported	LD50 (M) = approximately 1.65 (1.125-2.200) mg/kg salivation, diuresis, diarrhea, disoriented locomotion, chromado-cryorrhea, piloerection body tremors (only one sex was tested)	I	Minimum
Acute Oral LD50 - Mouse American Cyanamid #A-72-95 12/5/72	00037467	85.8% in corn oil	112227	LD50 (F) = 5.0 (4.0-6.3) mg/kg (only one sex was tested)	I	Minimum
Acute Dermal LD50 - Rabbit American Cyanamid #A-72-95 12/5/72	00037467	85.8%	112227	LD50 (M) = 1.0 (0.67-1.3) mg/kg (only one sex was tested)	I	Minimum
Primary Dermal Irritation - Rabbit American Cyanamid #A-72-95 12/5/72	00037467	85.8%	112227	All animals died within 24 hours after application of 0.25 ml (equivalent to 0.2225 g)		Minimum
Primary Eye Irritation - Rabbit American Cyanamid #A-72-95 12/5/72	00037467	85.8%	112227	All animals died within 24 hours after application of 0.1 ml (equivalent to 0.1105 g)		Minimum

Study/Lab/Study #/Date	MRID	Material	Accession Number	Results	Tox. Cat.	Core Classification
Acute Inhalation LC50 - Rat American Cyanamid #A-72-3 4/24/72	00044957	Technical	112227	LC50 (M) > 1.99 mg/L/7 hr (nominal dosage) (the actual dosage was not determined; the LD50 was not determined; and only one sex was tested)	II	Supplementary
Primary Dermal Irritation - Rabbit American Cyanamid #A-72-3 4/24/72	00044957	96.7%	112227	All animals died within 24 hours after dosing with 0.5 ml (equivalent to 0.5525 g)		Minimum
Primary Eye Irritation - Rabbit American Cyanamid #A-72-3 4/24/72	00044957	96.7%	112227	All animals died within 2-24 hours after dosing with 0.1 ml (equivalent to 0.1105 g)		Minimum
Acute Delayed Neurotoxicity - Hens Bio/dynamics #72S-788 11/10/72	00037472 (Final Report) 00045379 (Addendum)	Technical 86.5% a.i.	112227 112224	Negative for delayed neurotoxicity at 40 mg/kg, the only level tested (it is the LD50 for hens).		Minimum
Acute Oral LD50 - Rat American Cyanamid #A-72-96 12/5/75	00037468	15G in corn oil	112227	LD50 (M) = 11.7 (9.0-15.3) mg/kg (only one sex was tested)	I	Minimum

Study/Lab/Study #/Date	MRID	Material	Accession Number	Results	Tox. Cat.	Core Classification
Acute Dermal LD50 - Rabbit American Cyanamid #A-72-96 12/5/72	00037468	15G	112227	LD50 (M) = 10.2 (7.7-13.4) mg/kg (only one sex was tested)	I	Minimum
Primary Dermal Irritation - Rabbit American Cyanamid #A-72-96 12/5/72	00037468	15G	112227	All animals died within 24 hours after dosing with 0.5 mg.		Minimum
Primary Eye Irritation - Rabbit American Cyanamid #A-72-96 12/5/72	00037468	15G	112227	All animals died within 72 hours after dosing with 0.1 mg.		Minimum
Mutagenicity Testing:						
Mutagenicity - Ames American Cyanamid Agric. Division 4/12/78	00063209 GS-02	Technical (88.5% a.i.)	234103	Negative with or without microsomal activation in Salmonella typhimurium TA-1535, TA-1537, TA-98, TA-100 and E. coli WP-2-urvA.		Acceptable
Mutagenicity - Ames American Cyanamid Agric. Division 4/12/78	00063209 GS-02	Technical (88.5% a.i.)	234103	Negative with or without microsomal activation in Salmonella typhimurium TA-153o, TA-1538, TA-98, TA-100 and E. coli WP-2-urvA.		Acceptable

Study/Lab/Study #/Date	MRID	Material	Accession Number	Results	Tox. Cat.	Core Classification
Mutagenicity - DNA Repair American Cyanamid Agric. Division 4/12/78	0063209 GS-02	Technical (88.5% a.i.)	234209	Negative using E. coli PolA$^+$, PolA$^-$, WP-2, WP-2-uvrA$^-$ and Salmonella typhimurium TA-1978 and TA-1538.		Acceptable
Subchronic Testing:						
28-Day Feeding for ChE determination - Dog Cyanamid #A77-158 10/19/77	00063189	Technical (88.5% a.i.)		Dosage: 0.05 mg/kg No effect on RBCChE, PChE level was inhibited by 79% as compared to the control group. (only one dosage was tested)		Supplementary
30-Day Dermal - Rabbit FDRL #1611 7/17/73	00085169	Technical	112682	Dosages: 0.004, 0.02 and 0.10 mg/kg Systemic NOEL = 0.020 mg/kg; LEL = 0.10 mg/kg: edema and erythema were reported at this level. ChE activity was not determined.		Minimum
30-Day Dermal - Rabbit FDRL #1611 7/17/73	00085169	Counter 15G	112682	Dosages: 0.2. 1.0 and 5.0 mg/kg Systemic NOEL = 1.0 mg/kg LEL = 5.0 mg/kg (HDT): 3/4 (M) and 3/4 (F) died within 6 to 20 days. ChE activity was not determined.		Minimum

Study/Lab/Study #/Date	MPID	Material	Accession Number	Results	Tox. Cat.	Core Classification
90-Day Feeding - Rat Bio/dynamics #71R-725 4/9/73	00037469	Technical (86.5% a.i.)	not reported	Dosages: 0.25, 1.0, and 2.0 to 8.0 ppm ChE NOEL = 0.25 ppm (LDT) ChE LEL = 1.0 ppm Histology data were not reported; hence a systemic NOEL is undetermined. (See also the 2-year chronic feeding study in rats)		Supplementary
90-Day Feeding - Rat Bio/dynamics ~~#71R-725~~ 78-9345 11/28/79	GS-01	Technical (90.1% a.i.)	247985	Dosages: 0.125, 0.250, 0.500 and 1.00 ppm. ChE NOEL = 0.25 ppm ChE LEL = 0.500 (18% inhibition) Systemic NOEL = 0.25 ppm Systemic LEL = 0.500 based on a noted significant ($p < 0.05$) increase in the relative liver weight associated with an increase in the incidence of the liver extramedullary hematopoiesis (5%, 15% and 20% in the control, 0.500 ppm and 1.00 ppm respectively) in female groups. Biologically significant increases in the incidences of mesenteric and mandibular lymph node hyperplasia were noted at the high dose (1.0 ppm); however animals at the 0.500 ppm dose level were not examined for these microscopic lesions.		Minimum

Study/Lab/Study #/Date	MRID	Material	Accession Number	Results	Tox. Cat.	Core Classification
Chronic Testing:						
Teratogenic - Rat IBT#B1374-(B) 7/21/72	00082996	Technical	112227	Invalid (Canadian validation of 4/9/80)		Invalid
3-Generation Reproductio - Rat Bio/dynamics Inc. #71R-727 11/7/73	00085172 (final report) 00037473 (status report)	Technical	112682	Dosages: 0.25 and 1.0 ppm NOEL = 0.25 ppm; LEL = 1.0 ppm (HDT) based on the increased percentage of litters with offspring death in each of the 3 generations as compared to controls. (only 2 dosage levels were tested)		Minimum
6-Month Feeding - Dog FDRL; 1193 12/6/72	00041139 (final report) 0069502 (ChE data)	Technical (86.5% a.i.)	112225	Dosage: 0.0025, 0.01, 0.04 mg/kg/days; 6 days/wk for 26 weeks. ChE NOEL = 0.0025 mg/kg/day ChE LEL = 0.010 mg/kg/day (ChE inhibition was 26%, $p < 0.01$ for PChE, and 13% for RBCChE) A systemic NOEL could not be determined from this study although a decrease in ovary weight (both absolute and relative) was noted in all treated female groups. NOTE: Actual dosages could not be determined from the study as reported.		Supplementary

Study/Lab/Study #/Date	MRID	Material	Access Number	Results	Tox. Cat.	Co Classification
2-Year Feeding/ Oncogenicity - Rat Bio/dynamics #71R-725 7/31/74	00049236 (final report) 00045378 (11-month status report)	Technical (86.5% a.i.)		Dosages in ppm: 0.25, 0.1 and 4.0 (2.0 - 4.0 - 8.0 - 4.0) for female and 8.0 (2.0 - 4.0 - 8.0) for male. ChE NOEL < 0.25 ppm (LDT): dose-related RBCChE inhibition: 15%, 43% and 65% in females and 12%, 33% and 62% in males at the low-, mid-, and high-dose respectively as compared to controls. Systemic NOEL < 0.25 ppm (LDT): dose related mortality: 24% (M), 27% (F) at high-dose, 19% mid-dose (M) and 10% low-dose (M) above controls. Incidence of ocular lesions i.e. exophthalmia, film on eye, eye rupture and loss of lacrimation were noted in the high-dose females during the first year of the study period (exophthalmia was also noted in the low- and mid-dose females and at a lower incidence in the control females); and corneal scarring and cataracts were noted in both males and females of the high-dose group but also seen at a lower incidence in the mid-, low-dose and control groups. However, no microscopic examination was done on animals that died or were sacrificed moribund during the study; or for the 3-month interim sacrifices.		Supplementary

Study/Lab/Study #/Date	MRID	Material	Accession Number	Results	Tox. Cat.	Core Classification
				Only 5 animals/sex in the control group and 10 animals/sex in the treatment groups were microscopically examined and organ weights determined. Also lesions noted microscopically in the high dose group at high incidence (i.e. bone marrow hyperplasia) were not examined at the lower doses.		
18-Month Carcinogenicity - Mice Bio/dynamics #71R-728 2/4/74	00085170 (final report) 00045380 (12-month eye effect status report)	Technical (86.5% a.i.)	not reported	Dosages: 0.5, 2.0, and 8.0 ppm Negative for oncogenicity at 8.0 ppm Symptoms: alopecia and signs of disturbed balance. Ocular lesions: exophthalmia in males, corneal cloudness and opacity, and eye rupture. Only 15 animals/sex/group were histologically examined at termination (examination of the low and mid-dose groups included only liver, kidneys, heart and lungs).		Supplementary
Special Studies:						
Metabolism - Rat (M) American Cyanamid #2-402 12/7/73	00087695	Technical ^{14}C	not reported	Dosages: 0.8 mg/kg (specific activity 26.4 uCi/mg) 83.86% excreted in urine and 3.5% in feces within 168 hrs.		Acceptable

Study/Lab/Study #/Date	MRID	Material	Accession Number	Results	Tox. Cat.	Core Classification
				Maximum residues of ChE inhibiting compounds were found in liver and blood (1.4%) 6 hours after dosing. Residues of hydrolysis products reached a maximum in kidneys after 12 hours (1.2%). A slight residual activity (0.34%) remained in the liver at the end of the 168 hour observation period. All metabolites found in the rat have been previously identified in plant studies.		
Other Studies (Acute Toxicity of Terbufos related chemicals/metabolites)						
Acute Oral LD50 - Mouse American Cyanamid #A-72-36 6/9/72	00037477	S-(tert. butyl-thio) methyl 0,0-diethyl ester of phosphoro-thioic acid	112227	LD50 (F) = 2.2 mg/kg Vehicle: corn oil (death occurred as 0% or 100% between the lowest two dosages 1.53 and 3.13 mg/kg respectively; only one sex was tested)	I	Supplementary
Acute Oral LD50 - Rat IBT#A-1373 4/17/72	00037471	AC92553	not reported	LD50 (F) = 9,077 ± 1,2783 mg/kg Symptoms of the ChE inhibition. Animals that died has gastro-intestinal hemorrhage (only one sex was tested)	IV	Minimum

Study/Lab/Study #/Date	MRID	Material	Accession Number	Results	Tox. Cat.	Core Classification
Acute Oral LD50 - Mouse American Cyanamid #A-73-22 2/28/73	00085166	Bis (tert. butyl sulfinyl) methane (mixed isomers)	112682	LD50 (F) > 5000 mg/kg diuresis, dyspnea, prostration (only one sex was tested; and the LD50 was not determined)	IV	Minimum
Acute Oral LD50 - Mouse American Cyanamid #A-73-20 2/28/73	00085167	Tert. butyl (tert butyl sulfinyl) methyl sulfoxide	112682	LD50 (F) = 3970 mg/kg diuresis, convulsions (only one sex was tested)	III	Minimum
Acute Oral LD50 - Mouse American Cyanamid #A-73-21 2/28/73	00085168	Bis (tert. butyl sulfinyl) methane	112682	LD50 (F) = 3670 mg/kg diuresis, motor ataxia, convulsions (only one sex was tested)	III	Minimum

Discussion:

Technical Terbufos and Counter 15G (the only end use product for this chemical) are both acutely toxic (Category I) by the oral and dermal routes. The acute inhalation toxicity remains to be determined because the available data are only supplementary. Symptoms of acute cholinesterase inhibition were reported in all these acute studies. Gastrointestinal hemorrhage and exophthalmus were also noted especially when the technical material was administered orally.

*Acute Oral: The LD_{50} of technical Terbufos in rats ranged from 1.3 to 1.57 mg/kg in females and 1.6 to 1.74 mg/kg in males. The toxicity does not appear to be significantly affected by the solvent used. The acute oral LD_{50} for the formulation was 11.7 mg/kg in male rats (the only sex tested). Toxicity Category I.

*Acute Dermal: For the technical compound the LD_{50} in male rats was 1.0 mg/kg, and in male rabbits it was 1.1 mg/kg. The LD_{50} for the formulation was 10.2 mg/kg in male rabbits. These tests were not performed in females. Toxicity Category I.

*Acute Inhalation: The LC_{50} appears to be higher than 1.99 mg/L/7 hr. at 25°C in male rats tested with the technical material. The concentration of the chemical in the testing chamber was recorded as 1.99 mg/L. However, it is not clear from the data as reported if the concentration in the chamber is the nominal concentration or the actual mean Terbufos concentration determined analytically in air samples taken from the exposure chamber. In addition only one dosage was tested in this study.

The LC_{50} should be adequately determined in both males and females. At present, the toxicity category appears to be II for males. The acute inhalation test is waived for the formulation since it is a granular formulation intended for soil application. Due to the size of the granules and the method of application, exposure by inhalation is not anticipated.

*Primary Eye and Skin Irritation: Both the technical and the formulation are highly toxic to the extent that all rabbits tested in these studies died within 24 hours with the exception of the eye test performed with the formulation where the animals died within 72 hours. Apparently due to the acute toxicity of the chemical and the rapid death of the animals noted in these tests, the skin and eye irritation scores were not reported.

*Acute Delayed Neurotoxicity: The technical material was tested at 40 mg/kg in hens (the LD_{50} dosage). However, Terbufos did not produce signs of delayed neurotoxicity after the second 21-day dosing period (each bird was pre-treated with 10 mg/kg atropine 10-15 minutes before the second Terbufos dosing).

It is important to note that the oxygen analogue (metabolite) of Terbufos was also acutely toxic when administered orally to female mice, MRID 00037477 (Category I).

In Summary, due to the high acute toxicity of technical Terbufos and Counter 15G, both products are restricted to use by certified applicators. Signal word "Danger" and a skull and crossbones should appear on the label. Appropriate protective clothing should be worn by applicators.

The acute oral studies in male and female rats with the technical material do satisfy the requirement for an oral toxicity study when considered together. However an acute oral study in female rats is required with the formulation; an acute inhalation study is required with the technical material; and an acute dermal study in female rabbits is required with both the technical Terbufos and the Counter 15G formulation.

Mutagenicity

The Ames test on bacterial systems was performed with and without microsomal activation and the results were negative. Additional mutagenicity studies are required in mammalian systems, see Data Gaps Section.

Subchronic Studies

•A 30-day dermal study in rabbits (MRID 00085169) was performed with the technical material and Counter 15G. The Systemic NOEL was determined to be 0.02 mg/kg and 1.0 mg/kg respectively. However cholinesterase activities were not determined.

•A 28-day feeding study in dogs (MRID 00063189) was performed for determination of the cholinesterase activity. Only one dose, 0.05 mg/kg, was tested at a regimen of 6 and 7 days/week exposure. Both groups of animals showed similar levels of ChE activities with plasma ChE being significantly inhibited (79% inhibition) while no inhibition was observed in RBCChE activity.

•Two 90-days subchronic feeding studies were performed in rats. Both studies reflected a ChE NOEL of 0.25 ppm; however only one study (MRID GS-01) reflected a systemic NOEL of 0.25 ppm. A systemic NOEL could not be determined for the other study (MRID 00037469) because histological data were not reported.

In summary, additional subchronic studies with Terbufos are not required in light of the data already available.

Chronic Studies

•Teratology Studies: One IBT study in rats was submitted (MRID 00082996) and was determined to be invalid by the Canadians in their validation report of 4/9/80.

•Three-Generation study in rats. Only two dosages were tested, 0.25 and 1.0 ppm. This study (MRID 00085172) reflects a NOEL of 0.25 ppm and a LEL of 1.0 ppm based on the noted increase in the percentage of litters with offspring death in each of the three generations as compared to the controls.

•Six-month feeding in dogs: This study (MRID 00041139) reflected a ChE NOEL of 0.0025 mg/kg/day for both plasma and red blood cells cholinesterase inhibition. However no systemic toxicity was noted from the data as reported with the exception of a noted decrease in ovary weight (both absolute and relative) in all treated female groups as compared to the control group. However, it is not clear in this study how the dosage was mixed with the feed and how homogeneous the distribution of the test

substance was in the diet. In addition, an audit report on this study, dated May 1979, indicated that the raw data were not available to adequately support this study.

•Two-year chronic feeding/oncogenic study in rats: Both the ChE NOEL and the systemic NOEL in this study (MRID 00049236) appear to be lower than 0.25 ppm (LDT). Exophthalmus was noted in treated females in a dose-related fashion during the first year (MRID 00045378). This effect appeared to subside during the second year of the study period. However other eye lesions (corneal scarring and cataracts) were noted in both males and females of the high dose group (4 ppm for females and 8 ppm for males) at the end of the study. The oncogenic potential of Terbufos could not be assessed from this study because only too few animals of each group were histologically examined.

•Eighteen-month Carcinogenicity Study in Mice: Terbufos oncogenic potential could not be determined from this study (MRID 00085380) because too few animals (15/75 animals per sex per group) were histologically examined. Dose-related exophthalmia was noted in treated males during the first year (MRID 00045380). This effect subsided in the second year of the study period.

Exophthalmia appears to be related to Terbufos treatment. This lesion was noted in the acute oral toxicity study (MRID 00035121) with technical Terbufos, in the 2-year rat, and the 18-month mouse studies.

Ocular lesions and effects on the central and peripheral nervous system (brain, spinal cord, sciatic and optic nerves) should be examined during the life of the animals and at termination in any chronic study submitted in the future to fulfill a data gap. Adequate histology of the nervous system should be performed using a myelin specific dye.

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In conclusion, with the exception of the 3-generation reproduction study in rats which is classified as Core-Minimum, all the other available chronic studies are classified as supplementary and are considered as data gaps.

Metabolism

In male rats, Terbufos was rapidly excreted as the diethyl phosphoric acid and other polar metabolites (83%) in urine within 168 hours of administration. The compound and its metabolites were not noted to accumulate in tissues. (MRID 00087595).

This study is acceptable and satisfies the requirement for a metabolism study.

Antidote

Organophosphate poisoning is usually brought under control by atropine tablets or injection. Pralidoxime chloride may be effective as an adjunct to atropine.

Data Gaps:

*Technical Material

- Acute Dermal LD_{50} in Rabbits (F).

- Acute Inhalation LC_{50} in Rats (M&F).

- Two Teratology Studies in two different animal species; rats and rabbit are perferred.

- Two-Year Chronic Feeding/Oncogenic Study in Rats.

- One-Year Feeding Study in Dogs.

- Lifetime Oncogenic Study in Mice.

- Additional Mutagencity Studies:

1. In vitro mammalian cell point mutation [L5178Y (TK); or CHO (HGPRT); or V79 (HGPRT)].

2. In vitro cytogenetic damage: both chromosomal aberration and SCE (in CHO cells; or human lymphocytes; or other rodent/human cell lines/strains).

3. In vitro/in vivo primary hepatocyte repair for UDS testing both in vivo and in vitro exposure of cells to Terbufos.

4. In vivo cytogenetics test for chromosomal aberrations using bone marrow preparations of rats.

5. Dominant lethal test in rats or mice.

*Counter 15G Formulation

- Acute Oral LD_{50} in Rat (F).
- Acute Dermal LD_{50} in Rabbit (F).

NOTE: All the previously submitted chronic studies provide only supplementary data and cannot be used as a basis for tolerance assessment.

Tolerance Reassessment

Tolerances have been established for Terbufos on few major food and forage crops (CFR 180.352), see table below:

Crop	Tolerance*	Food Factor	mg/day (1.5 kg
Sugar, cane & beet (154)	0.05	3.64	0.00273
Corn, grain (68)	0.050	1.00	0.00075
Corn, sweet (40)	0.050	1.43	0.00107
Sorghum (147)	0.050	0.03	0.00002

TMRC

0.0046 mg/day (1.5 kg)

*Tolerances in/on corn forage and fodder, and in/on sorghum forage and fodder have been established at 0.5 ppm each, and in/on beets and sugarcane tops at 0.1 ppm. No residues were anticipated in milk, meat or eggs.

The tolerance of Terbufos on raw agricultural commodities was originally using a two-year rat cholinesterase no-observed-effect (NOEL) of 0.25 ppm (0.0125 mg/kg); MRID 00049236 & 00045378. This study has been reevaluated and reclassified as Core-Supplementary and a provisionary acceptable daily intake (PADI) was calculated using a six-month dog cholinesterase NOEL of 0.0025 mg/kg; MRID 00041139 & 00069502 (A. Mahfouz, 2/2/82 for PP#1F2433). The PADI was determined to be 0.000025 mg/kg/day with a provisionary maximum permissible intake (PMPI) of 0.0015 mg/day for a 60 kg individual. The current theoretical maximum residue contribution (TMRC) for Terbufos based on published tolerances is 0.0046 mg/day for 1.5 kg diets and uses 304.91% of the PADI.

The 6-month dog feeding study has been reevaluated during the preparation of this Registration Standard and has been classified as Supplementary because the actual dosages in the feed could not be determined from the data as reported. In addition, this study was also audited in May 1979 and questions were raised about the distribution of Terbufos in the feed, the actual concentration in the premix supplied by the sponsor, and the fact that the raw data were not available to adequately support the submitted study.

Consequently, reassessment of the established Terbufos tolerances should be performed as soon as a new chronic feeding study in rats or dogs is available. At the present time, the Agency will only grant those tolerances which do not result in more than an incremental increase of 1% or less in the TMRC.

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