

US EPA ARCHIVE DOCUMENT



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

MEMORANDUM

DEC 17 1981

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

DATE:

SUBJECT: Ametryne on Tanier and Yams, PP No. 1E2576 (Acc. No. 070360,
Caswell No. 431).

FROM: George Z. Ghali, Ph.D.
Toxicology Branch, HED (TS-769) *G. Ghali*

TO: P. Critchlow
Product Manager, No. 43
Registration Division (TS-767)

THRU: Christine F. Chaisson, Section Head *C.F. Chaisson*
Toxicology Branch, HED (TS-769)

William Burnam, Acting Branch Chief *W.B. Burnam*
Toxicology Branch, HED (TS-769)

Petitioner: The Interregional Research Project No. 4
Rutgers University
New Brunswick, N J 08903

Action Requested:

Establishment of a tolerance of 0.1 ppm for Ametryne residues on the raw agricultural commodities Tanier and Yams.

Recommendations:

Toxicology Branch recommends the establishment of the proposed tolerance at 0.1 ppm on the raw agricultural commodities Tanier and Yams.

Detailed Considerations:

1. Ametryne is listed on the memo of Dr. M. Ragoff, October 6, 1977 (See also D. Camp memo October 20, 1977) as a product containing nitrosamines.
2. The ADI was based on a NOEL of 50 ppm from a rat reproduction study with a safety factor of 100 fold and considered to be 0.025 mg/kg/day. This study was conducted by IBT and not yet validated, therefore, a Provisional Acceptable Daily Intake (PADI) was established on the basis of a NOEL of 1000 ppm from a subchronic 90-day feeding study in dog with a safety factor of 2000 fold and considered to be 0.0125 mg/kg/day.
3. The theoretical maximum residue contribution to the human diet from tolerances established under 40 CFR 180.258 up to this date is 0.0543 mg/day (1.5 kg of diet) or 7.24% of the ADI. /

4. Establishment of the proposed tolerance for each of the raw agricultural commodities tanier and yams will result in an increase of 0.00005 mg/day in the TMRC or 0.005% of the ADI. This is considered a miniscular increase and toxicologically supportable.
5. Ametryne contains less than 1 ppm of nitrosamine i.e. below validated sensitivity of the analytical method (1 ppm, R. Loranger, RCB). Toxicology Branch concluded that a cancer risk assessment is not essential in this case since the establishment of the current tolerances as proposed will not appreciably increase the percent of the ADI utilized, and the increase in cancer risk in this case will be inconsequential.
6. No further tolerances should be granted until all major data requirements are fulfilled and the IBT studies are validated since the outcome of this validation may indicate more data gaps.

Toxicology Profile:

(R. Coberly, memo 8/31/72, S. Sterling memo 11/19/79)

A. Technical Ametryne:

1. Acute oral toxicity
Rat LD₅₀ 1405 mg/kg
Mouse LD₅₀ 945 mg/kg
2. Acute dermal toxicity
Rabbit LD₅₀ > 10,200 mg/kg, IBT, validation is not available
3. Acute inhalation
Rat LC₅₀ > 27 mg/L
4. Primary eye irritation
mildly irritating
5. Subacute oral toxicity
90-day dog feeding, NOEL 1000 ppm
90-day rat feeding, NOEL 1000 ppm
90-day rat intubation, NOEL 100 ppm
6. Chronic feeding
2-year rat feeding, NOEL 1000 ppm, IBT, validation is not available
2-year dog feeding, NOEL 1000 ppm, IBT, validation is not available

7. Oncogenicity
Not available.
8. Teratogenicity
Rat, NOEL for F_{1a}-100 ppm
9. Reproduction
3-generation reproduction in rat, NOEL 50 ppm, LEL 100 ppm (IBT study, questionable effect), validation is not available.
10. Mutagenicity
Supplementary data were available to indicate that Ametryn was negative for mutagenic potential using microbial reverse mutation and rec-assay techniques. In vivo mammalian tests were deemed required as stated on page 26833 CFR Sec. 162.81, hazard to humans and domestic animals.

B. Ametryne Formulation Evik 80 W.

(J. Doherty, memo 2/15/78)

1. Acute oral toxicity
Rat, LD₅₀ 1766 (1350-2390) mg/kg,
Tox Category III, Core-minimum.
2. Acute dermal toxicity
Rabbits LD₅₀ 10.2 gm/kg
3. Acute inhalation toxicity
Rat 4 hours LC₅₀ > 1.35 mg/L, Tox Category II,
Rat not acceptable 4-hours LC₅₀ > 6.76 mg/L, Tox Category III,
Core Minimum.
Rat 4 hours LD₅₀ 2.22 mg/L, Tox category III, Core-minimal.
4. Primary eye irritation
Rabbit, reversible corneal opacity, iridial and conjunctivae
irritation, discharge, conjunctival hemorrhage, Tox category
II, Core-minimum.
5. Primary dermal irritation
Rabbits, mildly irritating, erythema, and edema, Tox category
III, Core-minimum.

C. Major Data Gaps:

1. Two oncogenicity studies
2. A second teratology study
3. Acceptable evaluation of mutagenic potential
4. All IBT studies are considered data gaps until validation is completed.

CFR 180.258

Ametryne

10/22/81

File last updated 10/22/81

ACCEPTABLE DAILY INTAKE DATA

RAT,Older	NOEL	S.F.	ADI	MPI
mg/kg	ppm		mg/kg/day	mg/day (60kg)
2.500	50.00	100	0.0250	1.5000

Published Tolerances

CROP	Tolerance	Food Factor	mg/day (1.5kg)
Bananas (7)	0.250	1.42	0.00533
Corn,sweet (40)	0.250	1.43	0.00536
Corn,grain (68)	0.250	1.00	0.00375
Grapefruit (65)	0.100	0.99	0.00149
Oranges (108)	0.100	2.17	0.00325
Pineapple (123)	0.250	0.30	0.00111
Potatoes (127)	0.250	5.43	0.02035
Sugar,cane&beet (154)	0.250	3.64	0.01364

MPI	TMRC	% ADI
1.5000 mg/day (60kg)	0.0543 mg/day (1.5kg)	3.62

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CROP	Tolerance	Food Factor	mg/day (1.5kg)
Yams (Yautia) (199)	0.100	0.03	0.00005
<u>Tanier</u> (214)	0.100	0.03	0.00005

MPI	TMRC	% ADI
1.5000 mg/day (60kg)	0.0544 mg/day (1.5kg)	3.62

Void

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ACCEPTABLE DAILY INTAKE DATA

Dog mg/kg	NOEL ppm	S.F.	PADI mg/kg/day	MPI mg/day (60kg)
25.000	1000.00	2000	0.0125	0.7500

Published Tolerances

CROP	Tolerance	Food Factor	mg/day (1.5kg)
Bananas (7)	0.250	1.42	0.00533
Corn, sweet (40)	0.250	1.43	0.00536
Corn, grain (68)	0.250	1.00	0.00375
Grapefruit (65)	0.100	0.99	0.00149
Oranges (108)	0.100	2.17	0.00325
Pineapple (123)	0.250	0.30	0.00111
Potatoes (127)	0.250	5.43	0.02035
Sugar, cane&beet (154)	0.250	3.64	0.01364

MPI 0.7500 mg/day (60kg) TMRC 0.0543 mg/day (1.5kg) % ADI 7.24

Current Action PP# 1E2576

CROP	Tolerance	Food Factor	mg/day (1.5kg)
Yams (Yautia) (199)	0.100	0.03	0.00005
<u>Taxier</u> (214)	0.100	0.03	0.00005

MPI 0.7500 mg/day (60kg) TMRC 0.0544 mg/day (1.5kg) % ADI 7.25
