

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: April 6, 1979

Caswell 188DD

SUBJECT: PP# 8F2081 proposing tolerances for the combined residues of the herbicide Metolachlor and its metabolites, in or on corn forage and fodder, fresh corn including sweet corn (kernels plus cobs, husks removed), popcorn (grain), and soybean forage and fodder.

FROM: Laurence D. Chitlik, Toxicologist
TOX/HED TS-769

JDE 4-30-79

*Smith
File petition*

TO: Willa Garner, PM #23
RD TS-767

Petitioner: Ciba-Geigy Corporation

Common Name: Metolachlor (formerly CGA-24705)

Product Name: Dual 6E - Reg. No. 100-583

Chemical Name: (2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methyl-ethyl) acetamide)

Related Petitions: 5G1553, 5F1606, 6G1708, 7F1913, 8F2098

Proposed Tolerance: Combined residues of the herbicide metolachlor and its metabolites determined as (2-((2-ethyl-6-methylphenyl)amino)-1-propanol) and (4-(2-ethyl-6-methylphenyl)-2-hydroxy-5-methyl-3-morpholinone), each expressed as parent metolachlor in or on the following agricultural commodities:

1. Corn forage and fodder	1.25 ppm
2. Fresh corn including sweet corn (kernels plus cobs, husks removed)	0.1 ppm
3. Popcorn (grain)	0.1 ppm
4. Soybean forage and fodder	2.0 ppm

Recommendations:

At this time, TOX notes several data deficiencies, including a rat two year feeding study. When data, as noted in the memo of L. Chitlik, 11/22/78, 7F1913, is submitted and reviewed, this tolerance proposal may receive further consideration.

Discussion

The memo of G. Werdig, 1/25/79 (7F1913) noted that studies conducted by Dr. E.K. Weisburger on various aromatic amines, demonstrated that various mono-substituted, di-substituted, and tri-substituted anilines are oncogenic to rats and mice. Furthermore, it was postulated in this memo that terminal residues of metolachlor included monochloroacetic acid and 2-ethyl-6-methylaniline. (This structure is similar to compounds tested by Dr. Weisburger, i.e. - 2,4-xylidine, 2,5-xylidine and 2,4,5-trimethylaniline which "were tested and found positive as oncogens.")

Donald Reed of RCB, memo of 2/5/79, refuted the postulation that these two metabolites would be present, "No detectable residues of the postulated metabolites, monochloroacetic acid and 2-ethyl-6-methylaniline, would reasonably be expected in soybeans from this use." The Ciba-Geigy letter of 1/13/79, (J.A. Norton to J. Cummings) referenced in the RCB memo stated, "The amide which must be cleaved to produce the aniline is very stable under most chemical and biological systems. The conversion of metabolites to the aniline has been attempted on parent compound and biological material treated with metolachlor by using strong base and acidic conditions and no aniline was formed."

RCB review of A. Smith, 8F2081, concluded that proposed eggs, milk, and meat tolerances of 0.02 ppm (7F1913) are sufficient to cover residues resulting from these proposed uses.

NOTE: This RCB draft was supplied to TOX by RCB, but at Ciba-Geigy's request, this review is now being held pending submission of additional residue chemistry data.

The TOX memo of L. Chitlik, 7F1913, 11/22/78, indicated that the unpublished TOX approved tolerances on soybeans at 0.1 ppm and meat, milk and dairy products at 0.02 ppm are based upon a 90-day rat feeding study (300 ppm NOEL) with a 2000 fold safety factor. Also noted in this review are the following points:

1. A rat, two-year feeding study is to be submitted before 3/15/79.
2. Pathology data from the 90-day dog feeding study is to be submitted on or before 2/1/79. (Note: addendum received 1/25/79).
3. Ciba-Geigy has initiated a 6-month study in dogs on 10/24/78.
4. Item 8(d) of this review also states "No additional tolerance proposals for metolachlor will be considered until after the two-year rat study and pathology data from the 90-day dog study have been submitted."

The proposed metolachlor tolerances of 0.1 ppm in sweet corn and popcorn (with food factors of 1.43 and 0.08% respectively) would theoretically contribute only 0.00215 mg and 0.00012 mg/kg/1.5 kg diet respectively. If residues resulting from this use are considered along with the existing tolerance on corn, TOX approved tolerances on soybeans, meat, milk and eggs and other proposed tolerance on sorghum, the TMRC is still only 0.0180 mg/day/1.5 kg diet or 4.0% of the ADI.

No new data was submitted in this action.

TOX/HED:ssr:RDInit:RLandolt:3/23/79

cc
W. W. Bitter
5/3/79

CFR 160.368

letolachlor

1/26/79

File last updated 1/26/79

ACCEPTABLE DAILY INTAKE DATA

RAT, Older NOLL	S.F.	PADI	MPI
mg/kg	ppm	mg/kg/day	mg/day/60kg
15.000	300.00	2000	0.0075
			0.4500

Published Tolerances

CROP	Tolerance	Food Factor	mg/day/1.5kg
Corn, grain(63)	0.100	1.00	0.00150

MPI	TMRC	% ADI
0.4500 mg/day/60kg	0.0015 mg/day/1.5kg	0.33

Unpublished, Tox Approved PP 5G1553, 5F1606, 6G1708, 7F1913

CROP	Tolerance	Food Factor	mg/day/1.5kg
Soybeans(148)	0.100	0.92	0.00138
Meat, inc poultry(39)	0.020	13.85	0.00415
Milk&Dairy, Products(93)	0.020	28.62	0.00858

MPI	TMRC	% ADI
0.4500 mg/day/60kg	0.0156 mg/day/1.5kg	3.47

Current Action BF2081, 8F2098, lacking data for TOX approval

CROP	Tolerance	Food Factor	mg/day/1.5kg
Corn, sweet(40)	0.100	1.43	0.00215
Corn, pop(39)	0.100	0.08	0.00012
Sorghum(147)	0.300	0.03	0.00014

MPI	TMRC	% ADI
0.4500 mg/day/60kg	0.0180 mg/day/1.5kg	4.00
