

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

Chem

Smith
File, petition

DATE: March 26, 1979

SUBJECT: PP #8F2098 proposing tolerances for combined residues of the herbicide Metolachlor and its metabolites in or on sorghum forage and fodder and sorghum grain. (Caswell No. 188 DD)

From: Laurence D. Chitlik, Toxicologist *JDC 4-20-79*
TOX/IED, TS-769

To: Willa Garner, Product Manager #23
Registration Division, TS-767

Petitioner: Ciba-Geigy Corporation
Common Name: Methlachlor (formerly CGA-24705)
Product Name: Dual 8E Reg. No. 100-597
Chemical Name: (2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl) acetamide)
Related Petitions: 5G1553, 5F1606, 6G1708, 7F1913, 8F2081

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 sorghum forage and fodder at 1.5 ppm and sorghum grain at 0.3 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, PP #7F1913 is submitted and reviewed, this tolerance proposal (metolachlor in or on sorghum forage, fodder and grain) may receive further consideration.

Discussion/Background

The memo of G. Werdig, 1/25/79, (PP #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 monochloro-acetic acid and 2-ethyl-6-methylaniline (This structure is similar to compounds tested by Dr. Weisburger, ie-2,4-xylidine, 2,5-xylidine and 2,4,5 trimethylaniline which "were tested and found positive as onocogens.")

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 Ceiba-Geigy letter of 1/31/79, (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, 8F 2098, concluded that proposed eggs, milk, and meat tolerances of 0.02 ppm (PP #7F1913) are sufficient to cover residues resulting from this proposed use on sorghum.

Note: This RCB draft was supplied to L. Chitlik, TOX, by RCB, but at Ciba-Geigy's request, the RCB review is now being held pending submission of additional data.

The TOX memo of L. Chitlik, PP #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. (Addendum received 1/25/79)
3. Ceiba-Geigy 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 tolerance of 0.3 ppm in or on sorghum grain (considering a food factor of 0.03%) would theoretically contribute only 0.00014 mg/day/1.5 kg diet. If residues from this use are considered along with the existing tolerance on corn, TOX approved tolerances on soybeans, meat, milk, and eggs, and other proposed tolerances on popcorn and sweet corn, the TMRC is still only 0.0180 mg/day/1.5 kg diet or 4.0% of the ADI.

No new TOX data was submitted in this action.

3/27/79
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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(6d)	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 8F2081, 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
