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

MEMORANDUM SEP 21 1982

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

TO: Robert Taylor (25)
Registration Division (TS-767)
and
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

THRU: Orville E. Paynter, Chief
Toxicology Branch
Hazard Evaluation Division (TS-769)

SUBJECT: Lasso; Alachlor, EPA Reg.#524-316. Response to Monsanto's Letter of 8/13/82: An Addendum to the Review of 7/20/82 and a Reevaluation of the Proposed Lasso Tolerances in/on Sorghum seeds, forage and fodder, PP#0F2338; corn forage and fodder, PP#0F2348; and sunflower seeds, PP#1F2447. CASWELL#11

Registrant: Monsanto Company
1101 17th St., N.W.
Washington, D.C. 20036

Monsanto's letter of 8/13/82 submitted in response to our review of 7/20/82 included the following 4 points:

1. The registrant is requesting the establishment of the previously proposed Lasso tolerances (see review of 7/20/82) in/on the following food and feed items:

Sorghum seeds - at 0.1 ppm.
forage & fodder - at 0.5 ppm.

Corn forage & fodder - at 0.5 ppm instead of the present tolerance of 0.2 ppm.

Sunflower seeds - at 0.5 ppm.

The registrant is also requesting that the petitions for tolerances in peanuts (PP#0F2313), sugarcane (PP#9F2144), cabbage (PP#9F2156) and potatoes (PP#1F2551) be held in abeyance.

2. Monsanto is proposing the calculation of the ADI based on a NOEL of 3 mg/kg/day in the dog and a 1000 fold safety factor. This NOEL, according to Monsanto's calculations, is obtained by extrapolation of the NOEL (10 mg/kg/day) noted in the 3-generations rat reproduction study (BD-77-422) to the dog. The extrapolation is based on interspecies comparison via surface area.

3. Monsanto is requesting the reassessment of the oncogenic risk for applicators based on the actual exposure (the actual number of acreage treated per year and the fact that Lasso is used only for preemergence weed control and is typically applied to an area only once each season), see Monsanto's letter of 8/4/82. The registrant is also requesting that the dietary exposure be determined on the basis of maximum detected residues level as presented in table 4, p. 18, Vol. I of Monsanto's report, RD#393, MSL-1983, submitted on 1/5/82.

4. Finally, the registrant indicated that the following studies have already been submitted for review to fill some of the data gaps listed in our review of 7/20/82. The studies submitted are as follows:

- Mutagenicity Studies (ET 80-0101), submitted on 8/4/82, MSL-2403, RD#433. This submission included the following:
  - Reverse Mutation Assay (replacement study of (IBT#8536-8852)
  - Recombination Assay (replacement study of (IBT#8536-8850)
  - Additional articles from the scientific literature on point - mutation & DNA damage assay.
- A 21-day dermal toxicity study in rabbits, submitted on 7/30/82, MSL-2404.
- Addendum to dermal penetration experiment in monkeys (R.D.#396, Vol. 8, 1/5/82), submitted on 7/27/82.

Recommendations:

1. The requested tolerances in/on sorghum seeds (0.1 ppm) and forage and fodder (0.5 ppm); sunflower seeds (0.5 ppm); and in/on corn forage and fodder (0.5 ppm instead of the present tolerance of 0.2 ppm) can be recommended conditionally. Full registration will be recommended upon receipt and favorable review of the new rat feeding/oncogenic study.

Toxicology Branch rationale for these recommendations is the following.

- The incremental dietary exposure from the proposed food uses in/on sorghum seeds and sunflower seeds represents increases of 0.15% and 0.67% respectively in the existing TMRC. The total increase in exposure as a result of these two new uses is very small (less than 1% of the TMRC, see attached printout and the 7/20/82 review) and the "incremental risk" is minimal.

- The oncogenic risk associated with the existing TMRC (0.0342 mg/day/1.5 kg food) is less than 10^{-8} (Mantel-Bryan). This risk remains less than 10^{-8} with the additional uses as the new TMRC becomes 0.0344 mg/day/1.5 kg food.

- Tolerances do exist for meat, milk, poultry and eggs (CFR 40, 180.249) and additional tolerances in animal feed items will not increase the residues in these food items.

- Determination of a NOEL for ocular lesions, a major concern to Toxicology Branch (see memo of 1/8/80 by E. Budd), appears to be resolved in a new rat chronic feeding study, see comment #2 below.

2. The proposed ADI calculation suggested in Monsanto's letter of 8/13/82 is unacceptable. Extrapolation of data for the ADI calculation should be performed directly from an animal species to man and not from one animal species to another then to man. Consequently, Toxicology Branch recommends that calculation of the ADI should await the results of the new rat chronic feeding study which according to Monsanto's letter of 6/11/82 appears to reflect a NOEL of 2.5 mg/kg/day for ocular effects (the unveal degeneration syndrome).

3. A reassessment of the oncogenic risk based on actual exposure figures will be performed as soon as the new rat chronic feeding/oncogenic study is submitted for review. However we are requesting that EFB perform a new Alachlor exposure assessment which should provide Toxicology Branch with maximum and minimum values for daily and yearly exposures. Monsanto's letter of 8/4/82 on applicator exposure and the attached report "Qualitative use assessment for Alachlor" generated by BFSD for Alachlor registration standard "Phase I" should be reviewed by EFB for the new applicator exposure assessment. Also exposure associated with the recommendation of the additional uses proposed in the present action should be considered.

We also note that the dietary exposure calculated by Monsanto used the maximum observed residues on racs. Our dietary exposure (worst case) used the theoretical maximum residues contribution (TMRC). A new dietary exposure will be calculated upon receipt of the new rat chronic study. However we note that the maximum observed residues presented on table 4, p. 18, Vol. I of Monsanto's report, (RD#393, MSL-1983) were reviewed by RCB's Linda Propst on 8/5/82 and she reported that the residues in/on peanuts were 0.05 ppm while Monsanto's value for this rac was 0.02 ppm.

4. The new mutagenicity studies, 21-day dermal toxicity study in rabbits, and the addendum to dermal penetration in monkeys recently submitted to fill these data gaps (listed in our memo of 7/20/82) are presently under review.

NOTE: Detailed reviews of the proposed tolerances are available in our memo of 7/20/82.

Amal Mahfouz 9/20/82

Amal Mahfouz, Ph.D.
Toxicology Branch
Hazard Evaluation Division (TS-769)

Attachments

WSD for LDC 9/20/82

TS-769:th:TOX/HED:AMahfouz:9-17-82:card 6

CFR 180.249 Alachlor 9/13/82

File last updated 9/13/82 Based on Da# 002174 (the 7/20/82 Review)

ACCEPTABLE DAILY INTAKE DATA

Dog mg/kg	NOEL ppm	S.F.	ADI mg/kg/day	MPI mg/day(60kg)
$$$$$.$$$	$$$$$$$$	$$.$	$$$$$.$$$$	$$.$$$$$$$

Published Tolerances

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Corn,all types(36)	0.200	2.51	0.00753
Soybeans (oil)(148)	0.200	0.92	0.00275
Beans,dry edible(10)	0.100	0.31	0.00047
Beans,lima(11)	0.100	0.19	0.00029
Peas(117)	0.100	0.69	0.00104
Potatoes(127)	0.100	5.43	0.00814
Cottonseed (oil)(41)	0.050	0.15	0.00011
Peanuts(115)	0.050	0.36	0.00027
Milk&Dairy Products(93)	0.020	28.62	0.00858
Meat,inc poultry(89)	0.020	13.85	0.00415
Eggs(54)	0.020	2.77	0.00063

MPI	TMRC	% ADI
$$$$$$$$$$ mg/day(60kg)	0.0342 mg/day(1.5kg)	0.00

****

Current Action 0F2338, 1F2447

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Sorghum(147)	0.100	0.03	0.00005
Sunflower(156)	0.500	0.03	0.00023

MPI	TMRC	% ADI
$$$$$$$$$$ mg/day(60kg)	0.0344 mg/day(1.5kg)	0.00

****