

For Reference

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: January 31, 1978

SUBJECT: EPA # 100-EUP-59, An EUP for Dual 8E and tank-mixes

FROM: Chan S-L Ph.D. Tox/RD

Sim-Lam Chan

B 2/14/78

TO: Ms. Zink L., Special Registration Section

The registrant/petitioner, Ciba Giegy Corp. requested for an Experimental Use Permit on corn for:

1. Dual 8E alone, ppl and PreE.
2. Dual 8E tank mixed with Bladex, ppl and PreE.
3. Dual 8E tank mixed with Banvel, PreE.
4. Dual 8E tank mixed with AAtrex + Paraquat-reduced tillage corn.
5. Dual 8E tank mixed with AAtrex + Roundup-reduced tillage corn
6. Dual 8E tank mixed with AAtrex, Post E.

Tolerances for all the above herbicides have been approved previously on fresh corn, corn grain, fodder and forage. These levels as listed in 40 CFR 180 are presented below:

1. Dual, Metolachlor; 180.368; 0.1 ppm in/on fresh corn and corn grain 0.75 ppm in/on corn fodder and forage (temporary).
2. Bladex, 180.307; 0.05 ppm in/on fresh corn and corn grain; 0.2 ppm in/on corn fodder and forage.
3. Banvel or Dicamba, 180.227; 0.5 ppm in/on corn grain, fodder and forage.
4. AAtrex, Agrazine, 180.220; 0.25 ppm in/on fresh corn and corn grain; 15 ppm in/on corn fodder and forage
5. Paraquat, 180.205; 0.05 ppm in/on fresh corn, corn grain, fodder and forage.
6. Roundup, glyphosate, 180.364; 0.1 ppm in/on grain crops; no tolerance has been established on corn fodder and forage but 0.2 and 0.4 ppm approved in/on grass forage and soybean forage respectively. As such a temporary tolerance of 0.2 ppm of Roundup. Should be permissible in/on corn fodder and forage.

Dual or Metolachlor has been adequately evaluated by Tox. Branch; see reviews on 5G1553 dated November 12, 1974 by B. Jaeger, on 5F1606 dated May 27, 1975. by L. Chitlick and 7F1913 dated March 21, 1977 and September 23, 1977 by D. Ritter. The product Dual 8E intended for this EUP is closely similar to Dual 6E, an EPA registered product for use on corn. In addition, the acute toxicity data on Dual 8E submitted are as evaluated below, sufficient for the purpose of an EUP label. This should be modified to read "Causes skin and eye irritation", instead of "Causes eye irritation only. The inert ingredient [REDACTED] has been cleared for agricultural application.

Inert ingredient information deleted.

All the formulations for the other herbicides proposed for testing as tank mixes are EPA registered products, approved for use on corn field. These included Bladex 80W and 4L, Banvel, AAtrex 80W, Nine-oTM, 4L and 4LC, Paraquat CL and Roundup. The PM for these products is Mr. R. Taylor.

In view of the above informations on the herbicides proposed for testing on corn we can see no objection to the requested EUP.

We would however like to point out to the registrant that Dual may be a potential alkylating agent whose alkylating potency should be determined. More importantly, every emphasis should be placed in the study on its oncogenic potential.

The registrant should be informed that any action on Atrazine is in temporary suspension (see memo by Dr. M. Rogoff dated October 20, 1976) and that Paraquat is an RPAR candidate.

Evaluation of Acute Toxicity Data on Dual 8E. Only the acute toxicity data on Dual 8E were submitted in support of this EUP. They are evaluated below:

1. The Acute Oral LD₅₀ Study (rats)
 IBT No. 8530-10822, October 28, 1977
 5 rats/sex/dose were treated at 6 dose levels.
 LD₅₀ = 2533.5 mg/kg (1888.5-3398.9 mg/kg) both sexes.
 LD₅₀ = 1350 - 2025 mg/kg for female rats.

Toxic signs: diarrhea, tremor, weakness, convulsion, diuresis, lacrimation, salivation, nasal discharge, hemorrhagic urination, ptosis, emaciation etc.

Necropsy: red lung, pale kidneys, red discolored pyrotic stomach lining, hemorrhaged lung.

Evaluation: Acceptable, Tox. Cat. III,
 Core minimum Std.

2. The Acute Dermal LD₅₀ Study (rabbits)
 IBT No. 8530-10822, October 28, 1977

A single sdose level of 3038 mg/kg, no mortality. (24 hr patch test on 3M + 3F)

Toxic signs: slight weight loss, well defined local erythema and edema, 2nd degree burn.

Necropsy: light colored liver, pale kidneys, depletion of body fat.

Evaluation: Acceptable, Tox. Cat. III
 Core minimum Std.

3. The Acute Inhalation LC₅₀ Study (rats)
 IBT No. 8562-10823, October 5, 1977

5M + 5F rats were exposed for 4 hour at levels of 0.22 and 0.94 mg/L of Dual 8E (gravimetric concentration). Animals were observed for 14 days.

LC₅₀ > 0.94 mg/L

Toxic signs: No untoward effects, no mortality

Necropsy: No tissue changes.

Evaluation: Acceptable, Tox Cat II, this is assigned in the absence of higher dose levels tested and may be revised accordingly upon presentation of studies with higher doses. This study may be classified as core-minimum Std.

4. The Primary Eye Irritation Study (rabbits):

IBT No. 8530-10822, October 21, 1977

0.1 ml of Dual 8E was applied to one eye each of:

3 rabbits --- unwashed eyes

3 rabbits --- eyes washed after 30 second.

The treated eyes were scored according to Draize.

Results:

Unwashed eyes: moderate corneal opacity, reversed in 7 days: ^{washed eyes} no corneal opacity; slight iris and moderate conjunctival effects reversed in 3 days.

Evaluation: Acceptable, Tox, Cat. II,
Core-Minimum Std.

5. The Primary Skin Irritation Study (rabbits)

IBT No. 8530-10822, October 21, 1977

0.5 ml of Dual 8E was applied to each of 6 rabbits in a 24 hour occlusion test. Animals were observed for 14 days.

Results: moderate erythema and edema and 2nd degree burns were seen at 72 hour.

Evaluation: Acceptable, Tox. Cat ~~II~~ (A typo, should be tox. Cat II, SLC, 3/28/78)
Core-minimum Std.

Validation of IBT Studies

The above 5 acute toxicity studies on Dual 8E were conducted by IBT. These studies have been validated by 2 teams of Ciba Giegy scientists in accordance with the procedure of certification of suspect data as set forth by EPA, see memo by D. Campt. dated January 3, 1978. Drs. J. A. Norton and J. T. Stevens audited the acute oral and acute dermal studies. Drs. R. J. Patterson and G. L. Rolofson checked the acute inhalation, the primary eye and skin irritation studies. In all these studies only a few minor differences were found between recorded original data and reported materials. These differences will not affect Tox. evaluations of the studies.

Recommendations:

The requested EUP can be toxicologically supported provided that residue levels for Dual and the other herbicides used in the tank-mixed so not exceed their respective level existing tolerance levels in/on corn grain, fodder and forage as determined by Chemistry Branch.

The registrant should be informed that Dual may be an alkylating agent whose alkylating potency should be determined. Special care should be given to examine the oncogenic potential of Dual.

EPA should inform Ciba Geigy that any action on Atrazine is temporarily suspended (Rogoff memo, October 20, 1976) and that Paraquat is on RPAR candidate.

The label should be modified to read "Causes skin and eye irritation" after the word "Warning".

All the acute toxicity data on Dual8E have been performed by IBT. These studies have however been validated by Ciba Geigy scientists in accordance with the procedure specified by EPA.

Chan S-L Ph.D.

JM