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

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MAY 24 1985

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Farm Worker Exposure Study; Terbufos (Counter®); Caswell #131 A; EPA Reg. # 241-238

TO: William Miller, PM # 16
Reg. Division (TS-767C)

FROM: Winnie Teeters, Ph.D. W. Teeters 5-22-85
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Tox. Brn., HED (TS-769C)

THROUGH: Laurence D. Chitlik, D.A.B.T.
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Tox. Brn., HED (TS-769C)
and
Theodore M. Farber, Ph.D.
Chief, Tox. Brn.
Hazard Evaluation Div. (TS-769C)

Action Requested: Review of Farm Worker Exposure Study with Aerial Application of Counter 15-G. This study is under the purview of Environmental Assessment Branch; Toxicology Branch reviewed only the toxicological aspects of the study and made a recommendation regarding labeling.

Recommendations: There was no indication of exposure to a loader, flagger or scouts as reflected in urinary excretion of phosphoric acid metabolites of terbufos (Counter®), but there was definite indication of exposure for 2 of 3 scouts on the first day of field re-entry (Day 3) following spraying, as reflected by significant (25-37%) depression of erythrocyte cholinesterase activity; plasma cholinesterase activity was not affected in the loader, flagger or scouts.

Although there were only three scouts used in this study to evaluate the effects of field re-entry, two showed evidence of compound absorption upon re-entry on the third day after the field was sprayed; therefore, Toxicology Branch, in consideration of these data, recommends against the proposed label change to permit re-entry on the third day posttreatment.

This action relates to a new use pattern and apparently the tolerance in corn remains the same. An incremental risk assessment for this new use pattern in reference to dietary exposure is, therefore, not warranted.

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Study Title: Farm Worker Exposure Study With Aerial Application of Counter 15-G.

Accession No.: 252762

Study Numbers: Project # 0402; Report #C-2370; Exp. # 5511

Sponsor/ Contracting Lab.: American Cyanamid Co./ Same

Report Date/ Submitted: 2-24-84/ 3-5-85

Test Material: Counter 15-G (terbufos, CL-92,000)

Test Animal: Man

Test Exposure: Exposure to a loader, flagger and scouts from preparation and spraying of 6.7 lbs./A. (1.0 lb. active ingredient/A.) of Counter 15-G.

Methods: Methods in the report appropriate to the parameters reviewed were copied and are attached hereto. The methods were reviewed and appeared satisfactory, except that the statistical comparison for evaluating an effect on cholinesterase activity was based on the mean of all pre-exposure values for all subjects and the mean of values for all three types of exposure (loader, flagger and scout) for all exposure/postexposure periods. This is not an appropriate comparison; types of exposure and days should have been separated and each persons's individual mean control value should have been used for comparison rather than a combined control value.

Quality Assurance: There was no statement regarding quality assurance procedures.

Results:

A. Urinary concentrations of terbufos metabolites.

Urinary samples were analysed for diethylphosphoric acid, diethylthiophosphoric acid and diethyldiphosphoric acid All results were less than the sensitivity of the methods, which was 0.1 ppm for each metabolite. These data indicate that there was not significant absorption of terbufos.

Urinary collection was for the day of exposure (24 hours) and for the following day (24 hours). This period appears adequate, since in a rat metabolism study (PP# 4F1496) 72% of administered radioactivity had been excreted in the urine within 24 hours and 80.3% within 48 hours.

For each urinary sample, the 24-hour volume was recorded and each was analyzed for creatinine as an indication of completeness of collection. These data were reported in Table

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IX, which has been reproduced on the next page. These results show a wide variability in creatinine excretion for the five subjects, especially for Scouts B and C; for example, Scout B's output at 4 days was only 49%, and at 8 days only 42% of his control creatinine excretion and Scout C's excretion on Day 3 was 165% but on Day 4 was only 55% of his control output. This degree of variability seems excessive for a parameter that is supposedly so constant that it has been used routinely to assure completeness of collection of a 24-hour urinary sample.

B. Cholinesterase activity of plasma and erythrocytes.

There was no indication of exposure reflected in the plasma cholinesterase activity values of any subject. Some subjects had values during exposure or postexposure periods that were slightly less than their own mean control value but in no instance was as individual value lower that a subject's lowest control value.

There was no indication in erythrocyte activity that the loader and the flagger had absorbed terbufos during their exposure (5 minutes for the loader and 15 minutes for the flagger), but there was an indication on Day 3 for each of the three scouts. The scouts each entered the treated field for the first time on the third day following spraying and entered again on the seventh day after apraying; each entry lasted for 30 minutes. Erythrocyte activity values on Day 3 were 63, 88 and 75% of individual mean control values for Scouts A, B and C, respectively. Scouts A and C definitely have depressed activity when their activity for this day is compared to their own mean control value; for Scout B, with only 12% depression, the effect is equivocal, but the trend is the same as for the other scouts. On subsequent Days 4, 7 and 8, there was no indication of exposure for any scout as reflected in erythrocyte activity.

The investigators stated that there was not a statistically significant ($p<0.05$) difference between mean values for preexposure and exposure/postexposure for plasma (4.70 vs 4.95 U/ml) or erythrocyte (12.81 vs 13.76 U/ml) activity of the flagger, loader or scouts. However, this is hardly the appropriate comparison since it combines <u>all</u> exposure/postexposure periods and <u>all</u> types of subjects. Exposure should logically be different for loader, flaggers or scouts, and for scouts, it is logical to expect exposure to be greater the sooner the field is entered following spraying. The investigators' comparison also does not take advantage of having control data for <u>each</u> individual.

<u>Conclusion</u>: In an experiment to assess farm worker exposure following aerial application of terbufos at a rate of 6.7 lbs/A., no evidence of exposure as reflected by the presence of metabolites in the urine (collected for 24 hours on the day

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Table IX: Summary of Urine Volumes and Creatinine Values[a)]

	Preexposure		Exposure and Postexposure							
			0-Day		1-Day		7-Days		8-Days	
Worker	Vol. (ml)	Creatinine (mg/24 hr)	Vol. (ml)	Creatinine (mg/24 hr)	Vol. (ml)	Creatinine (mg/24 hr)	Vol. (ml)	Creatinine (mg/24 hr)	Vol. (ml)	Creatinine (mg/24 hr)
Loader	1,040	2,142	1,410	2,820	1,130	1,955	-	-	-	-
Flagger	920	2,079	990	1,960	1,400	2,072	-	-	-	-
			3-Days		4-Days					
Scout A	900	1,692	900	1,926	860	1,565	660	1,320	1,020	1,479
Scout B	1,110	1,576	680	1,754	700	770	3,360	1,478	240	664
Scout C	2,050	1,271	3,740	2,094	2,360	700	2,650	954	3,360	941

a) - These are 24-hour urine samples. The creatinine work was performed by Pathological Medical Services, Lincoln, Nebraska. Normal range of values was considered to be 800-1800 mg creatinine/24 hour urine sample. Low values would indicate an incomplete sample while high values are possible with adults with larger muscle masses than normal.

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of exposure and for 24 hours of the following day) was found for a flagger, loader and three scouts; the latter re-entered the treated corn field on Days 3 and 7 following spraying. When exposure was assessed using depression of plasma or erythrocyte cholinesterase activity as the endpoints, 2 of 3 scouts definitely showed evidence of terbufos absorption only on Day 3, as reflected by 25-37% depression of erythrocyte activity and the evidence was equivocal for the third scout who had only 12% depression but the same trend as for the others. Plasma activity was not affected for any exposed subject.

Terbufos toxicology reviews

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