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

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

DATE: November 10, 1981

SUBJECT: Meeting with the Registrant on Dibromochloropropane (DBCP). Caswell No. 287.

FROM: Roger Gardner, Toxicologist
Toxicology Branch, HED (TS-769)

TO: Toxicology Branch File

On October 28, 1981, I met with representatives of Amvac Chemical Company, Henry Jacoby (Registration Division), and ken Bailey (Hazard Evaluation Division). The purpose of the meeting was to discuss a reproduction toxicity study (Warren, et al, 1981) and other data which might be required by the Agency in support of a tolerance for DBCP residues in peaches.

I discussed the Warren study in general terms stating that the study clearly associated histopathological changes in the testes, serum hormone level changes, and fertility with DBCP treatment in male rats. I also stated that the study did not clearly establish a no-observed-effect level (NOEL) with respect to fertility as shown by the failure of 2 of 5 treated males in the 1 mg/kg/day group (lowest dose tested) to sire litters.

At this point in the discussion the Registrant contended that the investigators believed their results would support a 1 mg/kg/day NOEL. I described the uncertainties about results at the 1 mg/kg/day level specific to fertility. I agreed with the Registrant that for histopathology and hormone levels the lowest dose had no effects, but fertility was not completely evaluated so that a NOEL could be established. The Registrant provided telephone numbers for two of the investigators in order that further information could be obtained to resolve uncertainties surrounding the apparent NOEL. I expressed my belief that the report clearly characterized the uncertainties.

(Note: On pages 60 and 61 of the submitted report results are described as follows:

> Two of the 5 animals treated with 1 mg/kg technical DBCP sired litters. One of the 3 animals which didn't sire a litter had pronounced morphological alternations in the testis.
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> Thus, 2 out of 5 of the 1 mg/kg technical DBCP treatment group and 1 out of 5 of the 5 mg/kg tehcnical DBCP treatment group did not sire litters. There is not apparent reason from histological, hormonal or reproductive organ weight studies to indicate a reason for these 3 animals not being able to sire. However, no assessment was made of the ability of the females to bear young.

> Thus, animals which show severe impairment of sperm production by histological criteria were not able to sire. Further studies need to be conducted to determine if any correlation exists between DBCP treatment at lower doses and fertility. (Emphasis added).

In view of the existing data, I informed the Registrant that a study should be conducted to determine a NOEL at lower doses for fertility. The study suggested involves mating treated male rats with two or more untreated females with known reproductive capability. At least two dosages, including 1 mg/kg/day were recommended. I emphasized the need for a study which is not as large as the standard multigeneration reproduction test usually required, since DBCP's effect on male reproduction is already characterized (with the exception of a NOEL).

It was agreed that this kind of study would not be needed unless results of residue analyses of peaches from trees grown in treated soils and worker exposure values were found to be above limits of detection.

On November 5, 1981, I received a call from Dr. Dwight Warren, principle investigator for the reproduction study. In that conversation Dr. Warren and I agreed that additional work is needed to determine a NOEL for fertility effects. He requested information on the Agency's testing guidelines for reproduction and teratology, and on November 6, I forwarded copies of F.R. 43, No. 163. Sections 163.83-3 and 163.83-4 (August 22, 1978).

Reference

Warren, D. W., N. Ahmad, and J. R. Wisner, Jr. 1981. The effects of 1,2-dibromo-3-chloropropane (DBCP), epichlorohydrin, and allyl chloride on male reproduction in the rat. Unpublished and proprietary. Final Report to Amvac Chemical Company Departments of Physiology and Biophysics and Anatomy. University of Southern California. Los Angeles, California.