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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

APR 18 1986

MEMORANDUM

SUBJECT: Triphenyltin Hydroxide: Comments on the Cannon 1976 study and Battelle 1981 study and justification of Toxicology Branch's position that triphenyltin hydroxide is not teratogenic in the rat at the dose levels tested.

FROM: John Doherty *Handwritten signature* 4/14/86
Toxicology Branch
Hazard Evaluation Division (TS-769)

TOX CHEM No. 896E
TOX Project No. 1647
1648
Record No. 170071

TO: Betty Shackelford
Product Manager Team 71
Registration Division (TS-767)

THRU: Edwin Budd
Section Head
Toxicology Branch
Hazard Evaluation Division (TS-769)

Handwritten notes:
Budd 4/16/86
4/17/86

In response to your inquiry concerning provision of a "detailed analysis of why the Cannon 1976 study and the Battelle 1981 study-both on teratogenicity-were deficient and have been rebutted" the following explanation should suffice.

In the original reviews of these studies they were assigned CORE MINIMUM classification (refer to the Toxicology Branch Chapter of the Registration Standard for triphenyltin hydroxide) indicating that the reports were of sufficient quality to be acceptable by the Agency to meet the study type requirement. No major procedural deficiencies were indicated but the study data presented indicated possible effects of the test material. The teratology studies were repeated by both the registrant and by the Agency's own testing facilities

in Research Triangle Park. None of the studies conducted subsequent to the 1981 Battelle study showed indications of the suspect lesions in carefully conducted studies which included postnatal development phases.

The nature of the suspect lesions involved (hydroureter, hydronephrosis and hydrocephalus) is recognized by Toxicology Branch (TB) to be precarious and difficult to interpret when noted. Sometimes it is in fact a result of the test material and other times it is only an artifact of the dissection procedure.

The development of the brain ventricles, kidney and ureters occurs late in gestation and these structures may in some cases differ in appearance among the fetuses if the dams from all test groups are not sacrificed within an appropriate time frame. Pups removed from the dams too early may have the appearance of the hydro conditions indicated. There is, however, no absolute way to determine if the increases in hydrocephalus and hydronephrosis in the Cannon 1976 study and the increases in hydroureter in the Battelle 1981 study were dissection artifacts.

In order to resolve whether the conditions noted in the 1976 and 1981 studies were indeed teratogenic or fetotoxic responses to the test material, TB required teratology studies which included postnatal developmental phases. These studies were specifically designed to assess the condition of the pups after allowing a specified period for development. Thus, any artifacts of dissection (or in fact any subtle change caused by the test material) would either worsen or be rectified during the postnatal development phase. The studies conducted since 1981 neither showed indications of TPTH dependent hydro conditions of the brain, kidney or ureters and no functional defects were noted in the pups which were allowed to develop to weaning.

TB is confident that the proper course was followed and that the additional testing conducted to more completely assess the possibility that TPTH causes the suspected lesions in the fetuses has clarified the problem. When all of the studies are taken together, the conclusion is that TPTH is not teratogenic at the dose levels tested.

The Cannon 1976 study and the Battelle 1981 study have not since been shown to be deficient. The implications from these studies that TPTH is teratogenic and/or fetotoxic have been rebutted by the results of the three teratology studies in rats conducted since 1981 which included postnatal development phases.