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

MEMORANDUM

MAR 23 1984

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

TO: Amy Rispin, Chief
SIS
Hazard Evaluation Division (TS-769)

THRU: Albin Kocialski, Acting Section Head
Section II, Toxicology Branch
Hazard Evaluation Division (TS-769)

PBK 3123184

SUBJECT: Consideration of Acute Toxicity in Risk Assessment of Pentachlorophenol (Wood Uses, PD-4).

We have been informed that two of the PD-4 exposure values (sum of dermal and inhalation exposure) for penta have been raised to the values of 0.12 and 0.25 mg/kg/day. At these exposures the margins of safety (MOS) for fetotoxicity are 23 and 12. In addition to our concern for the hazard of fetotoxicity, Toxicology Branch suggests, in view of the elevated exposure, that the adult acute toxicity of penta should receive thorough re-consideration. Our overall basis of concern is expanded in the discussion below.

In our memo to SPRD (Van Ormer, December 8, 1980) commenting on the acute toxicity of penta, we reference several values for the LD_{50} of penta by the oral or dermal route. The reported oral toxicity parameters for penta range rather widely, depending upon the species studied and the vehicle chosen. We point particularly to two of the values referenced in our memo of December 8, 1980:

1. LD_{50}, rat (acute oral) = 27.3 mg/kg (penta at 0.5% in Stanolex fuel oil; Deichman et al., 1942). Toxicity Category I.

2. Lowest human oral lethal dose estimate = 17.0 mg/kg (Dreisbach, 1980)

Of all the LD_{50} values reported, the value in fuel oil should have particular use for assessing exposures to penta in petroleum hydrocarbons. It may be realized that with an oral (or dermal) LD_{50} value in Category I, a General Use classification for penta formulations in hydrocarbon vehicles would require a waiver of CFR 40, Sec. 162.11 (p. 40, 1983), which requires that the pesticide not fall in Category I for General Use in either domestic or non-domestic applications.

Acute dermal toxicity parameters available for penta are not directly applicable to the formulations of interest. Our memo, however, quotes a value of 320 mg/kg for the dermal LD_{50} (in male rats) of penta in peanut oil. Calculating from the oral and dermal LD_{50} values in peanut oil, and the oral LD_{50} value in fuel oil (see 1980 memo), one may estimate, by proportion, that the dermal LD_{50} for penta in fuel oil should be approx. $27.3 \times \frac{320}{146} = 59$ mg/kg, a value in Toxicity Category I.

Accurate data on the dermal toxicity of penta formulations would assist proper risk assessment of acute toxicity.

The Dreisbach value for the lowest human oral lethal dose of penta (17.0 mg/kg) has been verified by personal communication with him, and is based on his statement that one gram (ca. 1000 mg/60 kg man) is a reasonable estimate for this value. At an exposure of 0.25 mg/kg/day (sum of dermal and inhalation) the estimate of MOS for human death becomes $\frac{17.0}{0.25} = 68$. The estimate of MOS for non-fatal human toxicity would, of course, range below 68. It should be noted, however, that in the case of penta the "largest dosage producing no illness is little less than the fatal dosage" (Wayland J. Hayes, Clinical Handbook on Economic Poisons, USDHEW, 1963).

As you are aware, the PIMS data indicate several instances of human fatalities from severe penta toxicity, for which the only known treatment is forced diuresis (Haley, 1978).

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