

201-16774



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A subsidiary of Occidental Petroleum Corporation

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February 10, 2009

The Honorable Lisa P. Jackson
U.S. Environmental Protection Agency
1200 Pennsylvania Ave., NW
Washington, D.C. 20460

**Attn: Chemical Right-to-Know Program
Dechlorane Plus (CAS: 13560-89-9)
Docket No.: 201-15897**

OFFICE OF THE
EXECUTIVE SECRETARY

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Dear Mr. Johnson:

Occidental Chemical Corporation (OxyChem) is pleased to submit an update to the IUCLID Data Set for Dechlorane Plus (CAS: 13560-89-9). The update includes summary results of the recently completed toxicology study, "Dechlorane Plus: Oral Repeat Dose Toxicity and Reproduction/ Developmental Toxicity Screening Study in Rats" (MPI Study No. 786-025). This study was undertaken by OxyChem as a commitment to the High Production Volume (HPV) Challenge Program. This study also responds to EPA's assessment that the previous Dechlorane Plus repeat dose study in rats was inadequate and that reproduction and developmental toxicity data were needed. Therefore, this combined repeat dose toxicity and reproduction/developmental toxicity study was conducted according to OECD Guideline 422 and in compliance with Good Laboratory Practice (GLP) regulations. The protocol for this study was reviewed by the EPA prior to initiation of the study (email from Dr. Ralph Northrop to Dr. William J. Brock, August 2007).

As described below, no compound-related toxicity was observed in any of the treated animals at any dose level, i.e., the no-observed-adverse-effect level (NOAEL) for Dechlorane Plus was 5000 mg/kg, the highest dose examined.

This study consisted of two phases, a 28-day repeat dose toxicity phase and a developmental and reproductive toxicity phase. Dose levels for both phases were 750, 1500 and 5000 mg/kg, and the test article was administered by gavage to male and female CD[®] [CrI:CD[®] (SD)] rats. Controls were treated with the vehicle, corn oil. The dose volume was 10 mL/kg/day. For both phases of the study, observations for clinical signs, morbidity, mortality, injury, body weight measurements and the availability of food were conducted for all animals.

For the Repeat Dose Toxicity Phase, in addition to the above observations, detailed neurobehavioral observations were performed approximately 1 to 2 hours post-dose weekly with Functional Observational Battery (FOB) and motor activity evaluations conducted prior to study initiation and during Week 4. Blood and urine samples for clinical pathology evaluations (hematology, coagulation, clinical chemistry, and urinalysis) were collected at termination. Animals were euthanized on Day 29, necropsy examinations were performed, organ weights were recorded and selected tissues were microscopically examined.

For the Developmental and Reproductive Toxicity Phase, rats were treated with the test article or vehicle for 63 days in males and 43-64 days in females. Following a 21-day pre-mating period, males and females of the same treatment group were paired for mating up to 14 days or until evidence of mating was observed. Females were examined daily for estrous cycle determination during the pre-mating and mating periods until evidence of mating was observed. On Gestation Day (GD) 20, selected females were euthanized and subjected to a complete necropsy, including a uterine examination in which the total number of implantations, early and late resorptions, viable and nonviable fetuses and the position of the cervix were recorded. The total number of corpora lutea on each ovary also was recorded. Gravid uterine weights were recorded and adjusted GD 20 body weights and body weight changes (GD 0-20) calculated. All fetuses were weighed, sexed, examined externally, and processed for visceral examination. Malformations and developmental variations were recorded. All surviving mated females not selected for GD 20 euthanasia and uterine/fetal evaluations were allowed to give birth (F₁). Observations of the offspring included survival at birth and through Lactation Day (LD) 4, and individual pup body weights and clinical observations on LD 0 and 4. On LD 4, surviving pups and dams were euthanized and subjected to a routine necropsy. At termination of the study, all surviving male animals were euthanized, subjected to a routine necropsy, and selected organ weights were recorded.

In the Repeat Dose Toxicity Phase, no effects were observed on clinical signs of toxicity, body weights, food consumption, neurobehavioral and FOB evaluations. In addition, no effects were observed on hematology, urinalysis, coagulation or clinical chemistry parameters, and no organ weight effects were observed. Other than the macroscopic and microscopic findings associated with gavage errors (see below), no compound-related pathological changes were observed in the treated rats.

In the Developmental and Reproductive Toxicity Phase, no effects were noted on clinical signs of toxicity, body weights or food consumption. No effects were observed on estrous cyclicity, reproduction and fertility indices or on parturition (gestation length, litter size), pup body weights, sex ratios or clinical findings through to LD 4. No effects were noted on GD 20 uterine implantation data, fetal body weights or fetal sex ratios. No fetal external and visceral malformations or variations were observed.

In both phases of the study, mortalities occurred across all dose groups (Table 1).

**Table 1: Total Mortality of Rats
Treated With Dechlorane Plus**

Dechlorane Plus Dose (mg/kg)	Total Mortalities*	
	Male	Female
Control	1/30	2/30
750	2/30	3/30
1500	2/30	1/30
5000	2/30	2/30

*Incidence of mortality/total numbers of rats in each group for both phases

These deaths were considered related to gavage injury or aspiration of the test article and not directly related to treatment. Microscopic lesions observed in the thoracic or pleural cavities consisted of adhesions, inflammation and fibrosis with evidence of esophageal perforations noted in some animals. In addition, microscopic findings were observed that were associated with an antigenic stimulus, immune response and/or a physiological stress response secondary to the presence of test article material in the thoracic cavity. These findings were not considered to be test article related as they were not dose dependent and were observed in animals with evidence of suspected gavage injury.

Overall, the mortalities noted in this study were unrelated to Dechlorane Plus administration but to gavage errors based on macroscopic and microscopic findings. In addition, the test article as formulated in corn oil was quite viscous which added to the difficulty of administration. Viscosity measurements of the Dechlorane Plus suspensions in corn oil used in this study was determined, and ranged from 60 cps for the vehicle (corn oil) to 5000-9000 cps for the high-concentration. Hence, the viscosity of the test article suspensions most likely contributed to the mis-dosing and mortalities observed in this study.

On the basis of these data, the No-Observable-Effect Level (NOEL) with Dechlorane Plus in both the Repeat Dose and Developmental and Reproductive Toxicity Phases of study was 5000 mg/kg/day, the highest dose level evaluated.

With the finalization of this study, OxyChem considers the HPV commitment to be complete for Dechlorane Plus.

Please contact Debbie Schober at 972-404-4969 should you have any questions.

Sincerely,

Stephen B. Kemp
Vice President
Health, Environment, Safety & Security

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