

**ABSOLUTE BIOAVAILABILITY OF SOIL LEAD IN MICROSWINE:
SOILS IDENTIFIED AS *FORT MADISON* AND *PLW-1***

MEDICAL RESEARCH PROJECT NO. 9905-001

PROTOCOL

Stine-Haskell Animal Welfare Committee No. CBT51-P

OBJECTIVE

The objective of this study is to determine the absolute bioavailability of lead from two different soils in microswine to aid in developing a site specific-clean-up goal.

SPONSOR AND TEST FACILITY

This study is sponsored by the Corporate Remediation Group of DuPont Chemicals, E. I. du Pont de Nemours and Company, Bellevue Corporate Center, Wilmington, Delaware. The study will be conducted at Haskell Laboratory for Toxicology and Industrial Medicine, E. I. du Pont de Nemours and Company, Newark, Delaware, in accordance with all applicable Good Laboratory Practice Standards. The sponsor's approval was effective the date the sponsor signed the Medical Research (MR) project.

STUDY DESIGN

The study design is as follows:

- fifteen male microswine will be used;
 - a predosing blood sample will be drawn from each animal for levels of background lead;
 - ten microswine will be dosed orally by gavage (five microswine/soil) with test soils containing 500 ppm (Fort Madison) or 4,000 ppm (PLW-1) lead (approximately 17 mg of lead/microswine);
 - five microswine will be given a single intravenous injection of lead acetate solution containing lead-dose equivalent to that contained in the gavage dose;
 - approximately 0.5 ml of blood will be drawn from each microswine at 0.5, 1, 2, 4, 8, 12, 24, 48, 72, 96, 120, 144, 192, and 240 hours after dosing;
 - blood will be collected in lead-free tubes containing heparin and stored at approximately -20°C until analysis; and
 - at sacrifice, liver and bone (both cortical and trabecular as well as whole femur) will be collected, weighed, and frozen at approximately -20°C.
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The program is monitored and administered by the laboratory veterinarian; data are maintained separately from study records.

D. Assignment to Groups

Healthy animals will be selected by computerized stratified-randomization such that there are no statistically significant differences among group body weight means. Microswine will be housed individually. Each animal will be assigned its own Haskell animal number and permanently identified by a number marked on the microswine's ear.

E. Animal Husbandry

After assignment to groups, animals will be identified with a cage card and housed in stainless steel cages. All microswine will be provided optimized test diets of approximately 340 gram/microswine/day. Deionized water will be provided *ad libitum*.

Animal rooms will be targeted at a temperature of $25 \pm 2^\circ\text{C}$ and a relative humidity of $50 \pm 10\%$.

F. Diet Preparation and Analysis

During the test period, microswine in each group will be fed Swine Basal mix (95%) (TD 93034).

This diet will be custom formulated by the manufacturer so that it contains complete normal nutrition for this species. The diet will contain $< 0.1 \text{ ug Pb/g}$.

Sucrose will be added to the diet and thoroughly mixed for a period of time adequate to assure homogeneous distribution in the diet. Once prepared, the diet will be refrigerated until used or discarded.

G. Body Weights

Microswine will be weighed twice per week unless experimental findings warrant a more infrequent weighing schedule. Concurrent with the collection of body weights, microswine will be individually examined and clinical observations will be recorded.

L. Data Analysis

The blood lead concentrations determined by atomic absorption will be used to calculate AUC (area under blood concentration versus time curve) and absolute bioavailability of lead. Individual animal data as well as the mean for six animals in each group will be reported.

M. Statistical Methods

Body weights and body weight gain will be analyzed by one-way analysis of variance. Appropriate statistical analysis will be performed on mean AUC values between oral and intravenous administrations.

SAFETY AND HOUSEKEEPING

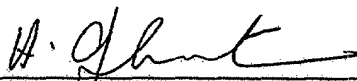
Good housekeeping practices will be used to avoid contamination of work areas and potential health hazards. Gloves will be worn when handling formulation, blood, animals, animal tissues, or analytical standards. Animal carcasses, feces, and diet will be incinerated.

RECORDS AND SAMPLE RETENTION

All original records will be retained at Haskell Laboratory, Jackson Laboratory (DuPont Chambers Works) or at the Records Management Center, E. I. du Pont de Nemours and Company, Wilmington, Delaware.

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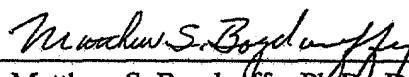
Approved:



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5/19/94

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