

Handwritten note

TOXICOLOGY ENDPOINT SELECTION DOCUMENT

013130

Chemical Name: Chlorpyrifos

PC Code: 059101

This document supercedes the TES document for Chlorpyrifos of 8/15/94.

Based upon a review of the toxicology database for the chemical listed above, toxicology endpoints and dose levels of concern have been identified for use in risk assessments corresponding to the categories below. A brief capsule of the study is presented for use in preparation of risk assessments.

Where no appropriate data have been identified or a risk assessment is not warranted, this is noted. Data required to describe the uncertainties in the risk assessment due to the toxicology database are presented. These include but are not limited to extrapolation from different time frames or conversions due to route differences. If route to route extrapolation is necessary, the data to perform this extrapolation are provided.

Reviewer: Alan C. Levy Date: 4-29-96

Branch Chief: L. M. Sanner Date: 4/29/96

Dermal Absorption Data: Study selected - guideline No.: Pharmacokinetics in human volunteers following single oral and dermal doses (85-3; not a guideline study).

Accession No.: 249203

Summary: Six human male subjects were orally dosed with 0.5 mg/kg of chlorpyrifos. In addition, five subjects were dosed once dermally with 5 mg/kg of chlorpyrifos. Plasma cholinesterase depression was observed by the oral route, but not by the dermal route. On the basis of urinary excretion of 3,5,6-trichloro-2-pyridinol metabolite, the minimum absorption orally is approximately 70% and dermally approximately 1%.

% absorbed: 1%

Acute Dietary Endpoint (One Day)

Study selected - guideline No.: 28-day study in humans (no applicable guideline)

Accession No.: 112118

Summary: In a study conducted at Albany Medical College (Coulston et al., 1972), human volunteers (4 males/dose group) were given

daily oral (tablet) doses of 0 (placebo), 0.014, 0.03, or 0.10 mg/kg chlorpyrifos technical. Blood was drawn twice preexposure for baseline values; at 1, 3, 6, and 9 days of treatment for the 0.1 mg/kg/day dose group; and at additional posttreatment days for the 0.03 and 0.014 mg/kg/day dose groups. Plasma cholinesterase activity was measured.

Endpoint and dose for use in risk assessment: After 1 and 3 days of treatment, the mean plasma cholinesterase value was not significantly decreased at any dose level as compared to the baseline measurement. NOEL = 0.10 mg/kg/day; an uncertainty factor of 10 should be used.

This risk assessment is required.

Short Term Occupational or Residential Exposure (1 to 7 Days)

Study selected - guideline No.: 28-day study in humans (no applicable guideline)

Accession No.: 112118

Summary: In a study conducted at Albany Medical College (Coulston et al., 1972), human volunteers (4 males/dose group) were given daily oral (tablet) doses of 0 (placebo), 0.014, 0.03, or 0.10 mg/kg chlorpyrifos technical. Blood was drawn twice preexposure for baseline values; at 1, 3, 6, and 9 days of treatment for the 0.1 mg/kg/day dose group; and at additional posttreatment days for the 0.03 and 0.014 mg/kg/day dose groups. Plasma cholinesterase activity was measured.

Endpoint and dose for use in risk assessment: After 1 and 3 days of treatment, the mean plasma cholinesterase value was not significantly decreased at any dose level as compared to the baseline measurement. NOEL = 0.10 mg/kg/day; an uncertainty factor of 10 should be used.

This risk assessment is required.

Intermediate Term Occupational or Residential Exposure (1 Week to Several Months)

Study selected - guideline No.: 28-day study in humans (no applicable guideline)

Accession No.: 112118

Summary: In a study conducted at Albany Medical College (Coulston et al., 1972), human volunteers (4 males/dose group) were given daily oral (tablet) doses of 0 (placebo), 0.014, 0.03, or 0.10 mg/kg chlorpyrifos technical. Blood was drawn twice preexposure for baseline values; at 1, 3, 6, and 9 days of treatment for the

0.1 mg/kg/day dose group; and at additional posttreatment days for the 0.03 and 0.014 mg/kg/day dose groups. Plasma cholinesterase activity was measured.

Endpoint and dose for use in risk assessment: After 6 and 9 days of treatment with chlorpyrifos, significant plasma cholinesterase inhibition was observed for the 0.1 mg/kg/day treatment group. Mean values were 43% lower than baseline at 6 days and 64% lower than baseline at 9 days. NOEL = 0.03 mg/kg/day; an uncertainty factor of 10 should be used.

These risk assessments are required.

Cancer Classification and Basis: E, not a carcinogen

RfD and basis: 0.003 mg/kg/day, based upon plasma cholinesterase inhibition

NOEL for critical study: 0.03 mg/kg/day

Study type - guideline No.: 28-day study in humans (no applicable guideline)

Accession No.: 112118

Acute Toxicity

Guideline	Test	Results	Category
81-1	Oral LD ₅₀ ; rat (Acc. No. 112115)	163 mg/kg males; 137 mg/kg females	II
81-2	Dermal LD ₅₀ ; rat (Acc. No. None)	202 mg/kg	II
81-3	Inhalation LC ₅₀ ; rat (Acc. No. 257590)	LC ₅₀ > 0.2 mg/L (nominal concentration) Note: Supplementary	I
81-4	Eye Irritation; rabbit (Acc. No. 112115)	Slight irritation	II
81-5	Dermal Irritation; rabbit (Acc. No. 112115)	Slight irritation	III

81-6	Dermal Sensitization; guinea pigs (MRID No. 0095497)	non-sensitizing	
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