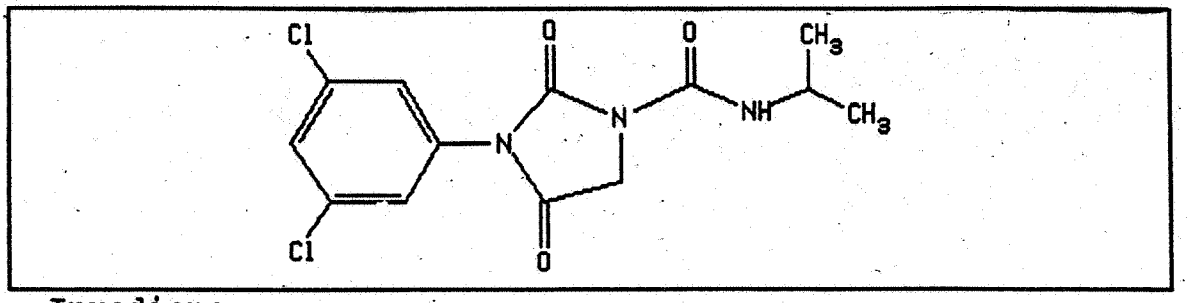
3-29-95

TOXICOLOGY ENDPOINT SELECTION DOCUMENT

Chemical Name: **IPRODIONE**



Iprodione

PC Code: **079401**

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 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: Linda Lee Ray C Date: 3/29/95

Branch Chief: Brian Gomez Date: 3/29/95

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Dermal Absorption Data (If available)

MRID:--none

% absorbed: assume 100%

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Acute Dietary Endpoint (One Day)

Study Selected - Guideline No.: --83-3(a)/83-3(b)

MRID No.: --431291-01/243707& 246792

Summary (Enter Standard Executive Summary or equivalent): -- In the developmental toxicity study in rabbits, Iprodione was tested at dose levels of 20, 60, and 200 mg/kg/day. The maternal NOEL was 20 mg/kg/day, the LEL 60 mg/kg/day, based on ↓ body-weight gain, loss of body weight; ↑ number of abortions at 200 mg/kg/day [7/18 aborted between gestation days 17 and 23; dosed on days 6-18]. Developmental NOEL was 60 mg/kg/day, the LEL was 200 mg/kg/day, based on skeletal variations [13th rib, sternebrae maligned]. The study is classified Core Minimum.

NOTE: A previous rabbit study in which doses of 100, 200, and 400 mg/kg/day [in 1% CMC; dosed on days 6-16] were used showed significant maternal mortality at 400 mg/kg/day [9/17; days 21-27]. The incidence of skeletal variations [ossification retardation] was significantly greater at all dose levels compared to the control and dose-related. At the low dose, the % of fetuses with at least 1 sternebra unossified was slightly but statistically significantly greater than in the control fetuses. Dosing did not encompass the entire period of organogenesis [dosed on days 6-16 of gestation]. There was a dose-related decrease in maternal body weight gain during dosing. Study classified Core Supplementary.

Endpoint and dose for use in risk assessment: - developmental NOEL = 60 mg/kg/day; increased abortions and skeletal variations

Comments about study and/or endpoint: - With regard to the question of whether the low dose in the supplementary study more appropriately describes the NOEL, since dosing in the supplementary study did not encompass the entire period of organogenesis and the fact that the slight but significant increase in skeletal variations at the 100 mg/kg/day dose level [lowest dose tested in the study] is comparable to the findings in the other study, the appropriate NOEL for use in the assessment is 60 mg/kg/day.

This risk assessment is required.

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

Study Selected - Guideline No.: 82-2

MRID No.: 420232-01

Summary (Enter Standard Executive Summary or equivalent):

DERMAL EXPOSURE - 21-day dermal toxicity study in rabbits: Dose levels of 0, 100, 500, and 1000 mg/kg/day; NOEL = 1000 mg/kg/day, HDT.

Endpoint and dose for use in risk assessment: none

Comments about study and/or endpoint: none

This risk assessment is not required.

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

Study Selected - Guideline No.: 82-2

MRID No.: 420232-01

Summary (Enter Standard Executive Summary or equivalent):

DERMAL EXPOSURE - 21-day dermal toxicity study in rabbits: Dose levels of 0, 100, 500, and 1000 mg/kg/day; NOEL = 1000 mg/kg/day, the LEL > 1000 mg/kg/day. No mortalities or clinical signs of toxicity; no adverse effect on body weight, food consumption, organ weights, clinical pathology, organ weights.

Endpoint and dose for use in risk assessment: none

Comments about study and/or endpoint: -- none

This risk assessment is not required.

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Cancer Classification and Basis: This chemical has been classified by the HED CPR Committee as a Group B2 - Probable Human Carcinogen, based on evidence of tumors in both sexes of the mouse and in the male rat, and that for the purpose of risk characterization, a low dose extrapolation model be applied to the animal data for the quantification of human risk (Q_1^*). The CPRC

recommended that the Q_1^* be determined for the combined hepatocellular adenoma/carcinoma for both sexes of the mouse and also for the testicular tumors in the male rat.

Q_1^* = 8.7×10^{-3} ♂♂/5.07×10^{-3} ♀♀ combined hepatocellular adenoma/carcinoma [mouse]
= 4.39×10^{-2} testicular tumors [rat]

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RfD and basis: An RfD of 0.06 mg/kg/day is derived using a NOEL of 6.1 mg/kg/day and an uncertainty factor of 100; NOEL established from a 2-year feeding study in rats. LOEL = 12.4 mg/kg/day, based on histopathological changes in the reproductive system of males and effects on adrenal glands in both sexes.

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Toxicity Categories: Guideline No.: §81-1 acute oral [III] - ≈4 g/kg
§81-2 acute dermal [III] - > 1 g/kg
§81-3 acute inhalation [III] - > 3.29 mg/L/4 hrs
§81-4 primary eye irritation [III]
§81-5 primary dermal irritation [IV]
§81-6 dermal sensitization [non-sensitizing]

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