OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

014466

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF PREVENTION, PESTICIDES, AND TOXIC SUBSTANCES
WASHINGTON, D.C. 20460

This revised report reflects a change from the previous HIARC report only in the selection of long-term dermal and inhalation end points and identification of datagaps. No other changes were made.

DATE: February 8, 2001

MEMORANDUM

SUBJECT: *DINOCAP* - **Report #2** of the Hazard Identification Assessment Review Committee.

FROM: Paul Chin, Ph.D. Paul Chin 2/8/01
Reregistration Branch I
Health Effects Division (7509C)

THROUGH: Jess Rowland, Co-Chair Jess Rowland 2/8/01
and
Elizabeth Doyle, Co-Chair E.A. Doyle 2/8/01
Hazard Identification Assessment Review Committee
Health Effects Division (7509C)

TO: William Hazel, Risk Assessor
Reregistration Branch I
Health Effects Division (7509C)

PC Code: 036001

On December 1, 1999, the Health Effects Division's Hazard Identification Assessment Review Committee (HIARC) evaluated the toxicology database of **dinocap** and selected the toxicological endpoints for acute and chronic dietary, occupational, and residential (dermal and inhalation) exposure risk assessments (Report dated Feb. 23, 2000, HED Doc. # 014006).

At the HIARC meeting (Dec. 1, 1999), it was reported that there was no long-term dermal or inhalation exposure based on the current use pattern. However, the only dinocap use still registered in the U.S. is the use on ornamentals in greenhouses. Such uses often result in long-term occupational exposure. Therefore, on December 19, 2000, the HIARC **revisited** dinocap to select long-term dermal and long-term inhalation endpoints for risk assessment purposes.

Committee Members in Attendance

Members present were: William Burnam, Elizabeth Doyle, Pamela Hurley, Elizabeth Mendez, Yung Yang, Jess Rowland, Ayaad Assaad, Jonathan Chen and Brenda Tarplee.

Member in an absentia: David Nixon.

Data evaluation prepared by: Paul Chin, Reregistration Branch I.

Also, in attendance were: William Hazel and Whang Phang, RRB1.

Data Evaluation/Report Presentation Paul Chin 2/8/01

Paul Chin
Toxicologist

1. INTRODUCTION

On December 1, 1999, the Health Effects Division's Hazard Identification Assessment Review Committee (HIARC) evaluated the toxicology database of **dinocap** and selected the toxicological endpoints for acute and chronic dietary, occupational, and residential (dermal and inhalation) exposure risk assessments (Report dated Feb. 23, 2000, TXR # 014006).

At the HIARC meeting (Dec. 1, 1999), it was reported that there was no long-term dermal or inhalation exposure based on the current use pattern. However, the only dinocap use still registered in the U.S. is the use on ornamentals in greenhouses. Such uses often result in long-term occupational exposure. Therefore, on December 19, 2000, the HIARC **revisited** dinocap to select long-term dermal and long-term inhalation endpoints for risk assessment purposes.

The Health Effects Division (HED) FQPA Safety Factor Committee met on March 13, 2000 to evaluate the hazard and exposure data for dinocap and recommended that the FQPA safety factor (as required by the Food Quality Protection Act of August 3, 1996) be retained at 10x when assessing the risks posed from the use of this pesticide (HED DOC. # 014071).

2. HAZARD IDENTIFICATION

2.1 Acute Reference Dose (RfD)

2.1.1 Subpopulation (Females 13+)

Study Selected: Developmental Toxicity Study in Mice Guideline #: 83-3(a)

MRID No.: 41313001

Executive Summary:

In a developmental toxicity study (MRID No. 41313001), Dinocap (94.4% a.i.) suspension in an aqueous 1% Tragacanth Gum was administered by gavage to CD-1 (ICR) BR mice (24/dose) at 0, 4, 10 or 25 mg/kg/day from gestation days 6 through 15. One group of 12 presumed pregnant females underwent caesarean section while the other 12 pregnant females were allowed to deliver naturally.

There were no maternal deaths. No clinical signs or post mortem observations were attributed to test article administration. Although not statistically significant, the body weight in the high-dose animals (25 mg/kg/day) was 5% lower than the controls on day 18 of gestation. In this group, the body weight gains were 7 and 11% lower than the controls from gestation days 6-15 and 0-18, respectively. **The NOAEL for maternal toxicity is 10 mg/kg/day; the LOAEL is 25 mg/kg/day based on the slight decrease in body weight and body weight gains.**

Although not statistically significant, dinocap at 25 mg/kg/day caused the following: reduction in numbers of corpora lutea, implantation size, litter size, and the percent of dams with any resoprtions. The number of total resorption and dead or resorbed conceptuses/litter in the high-dose animals were increased ($p<0.05$) when compared to the controls. In addition, dinocap at 25 mg/kg/day caused the following when compared to the controls: reduction in live fetal body weights (29% less than the controls, $p<0.01$); increased incidence of cleft palate ($p<0.01$), "eye lids open" ($p<0.01$), and head tilt; and an effect on swimming performance ($p<0.01$) (as measured by mice which sank and required rescue or swam on their side).

In the 10 mg/kg/day group, the number of total resorption was increased ($p<0.05$) and live fetal body weights were decreased (7% lower than the controls, $p<0.05$). However, these differences from control groups are considered to be of little or no toxicological significance. In the 10 mg/kg/day group, in addition, a slight (non-significant) increased incidences in cleft palate and eyelids-open occurred relative to the control group. Due to the absence of any occurrence in either concurrent or historical controls, the NOAEL is set conservatively at 4 mg/kg/day.

Natural delivery data showed that viability index, number of live precull on day 4 divided by number of live on day 1, was decreased ($p<0.01$) at 25 mg/kg/day (87% versus 97-100%) in the control and two lower dose groups. Lactation index was reduced ($p<0.01$) in the 4 mg/kg/day group only. However, this was primarily due to 8 pups from one litter dying by day 7 of weaning.

The NOAEL for developmental toxicity is 4 mg/kg/day; the LOAEL is 10 mg/kg/day based on the slight (non-significant) increase in incidences of cleft palate and eyelids-open relative to the controls.

This study is classified as ACCEPTABLE/NONGUIDELINE and does not satisfy the guideline data requirement for a developmental study (83-3a) in mice. The study was designed to answer specific question (the inner ear formation). The Agency requested that the registrant perform a "modified" developmental toxicity study in mice in order to elucidate developmental toxicity potential of purified dinocap (Q. Bui of the Agency to D. Edwards, dated 10/19/88, Tox. Doc. No. 007457).

Dose and Endpoint for Risk Assessment: **The NOAEL for developmental toxicity is 4 mg/kg/day; the LOAEL is 10 mg/kg/day based on the** slight (non-significant) increase in incidences of cleft palate and eyelids-open relative to the controls.

Uncertainty Factor(s): An uncertainty factor of 100 was applied to account for inter-species extrapolation (10 x) and intra-species variability (10 x).

Comments about Study/Endpoint/Uncertainty Factor(s): This endpoint is appropriate for females 13+ subpopulation only since the end point is an in utero affect.

There is evidence to suggest that **purified** dinocap (94.4% a.i.) is a developmental toxicant in mice at doses which were not maternally toxic (see executive summary described above). However, **technical** dinocap (84% a.i.) is also a developmental toxicant in mice at doses which were maternally toxic (Rogers J. M. et al. 1986, EPA's Developmental Biology Division/HERL. The doses used in this study were 5, 10, 20, 40, 80, and 120 mg/kg/day. There were no live fetuses at the 120 mg/kg dose level. Dose-related decreases in gravis uterus weight and fetal weight were significant at all remaining doses of dinocap. Cleft palate was found in fetuses at 5 (0.4%), 20 (23.6%), 40 (75.7%), and 80 (74.1%) mg/kg/day. There was also a dose-related increase in supernumerary ribs, but a low frequency of exencephaly and umbilical hernia at high doses. The developmental toxicity potential of dinocap was thus demonstrated at doses well below those causing maternal toxicity (LOAEL = 80 mg/kg as characterized by significant decrease in weight gain) (HED Doc. 007456, Nov 25, 1987). The LOAEL for developmental toxicity is < 5 mg/kg/day (LDT).

Since the new formulation is the technical product with 92.2% a.i., the HIARC selected the study conducted with the new formulation.

ACUTE RfD (females 13+) :	$\frac{\text{4 mg/kg (NOAEL)}}{\text{100 (UF)}} = 0.04$ **mg/kg**

2.1.2 General Population

Dose and Endpoint for Risk Assessment: No appropriate endpoint was identified for this population group because there were no effects attributable to a single dose was identified in oral toxicology studies including developmental toxicity studies in mice and rabbits.

2.2 Chronic Reference Dose (RfD)

The following RfD was established in 1994.

Study Selected: Chronic Feeding Study - Dog Guideline **#:** 83-1b

Accession No.: 247957

Executive Summary:

In a chronic toxicity study (Accession No. 247957), technical dinocap (78% a.i.) was administered to Beagle dogs (4/sex/dose) in the diet at levels of 0, 15, 60 or varying levels

of 120-240 ppm (0, 0.375, 1.5 or 3-6 mg/kg/day based on a conversion factor of 1 ppm = 0.025 mg/kg/day) for 2 years. [The test compound in the high dose group was fed at 240 ppm for 1 week, removed completely from the diet and restarted at 120 ppm for 4-30 weeks, increased again to 240 ppm for 11 days, removed completely, and then restarted at 180 ppm for 33-61 weeks.]

Treatment of dogs with varying levels of 120-240 ppm of dinocap was lethal. Four dogs (2 males and 2 females) died during the first 43 weeks. One died from unexplained causes and the other 3 deaths were related to dinocap treatment. The remaining 4 dogs had significant reduction in body weights and food consumption and they were sacrificed during week 62 because of weight loss and poor condition. Other compound related effects included occasional ataxia and clonic convulsions, salivation, decreased activity, and rapid and labored respiration.

Ocular examination revealed changes in the tapetum, retina and ocular disc of all 4 high level dogs examined (4 died before examination) and 6/8 of these dogs had histologic retinal atrophy.

The only treatment related effects noted in dogs fed 60 ppm of dinocap were **ophthalmoscopic changes** in 7/8 dogs and **histologic retinal atrophy** in 3/8 dogs.

Levels of 15 and 60 ppm of dinocap did not have an effect on oxidative phosphorylation in liver mitochondria; mitochondria from dogs in the high level were not tested.

Under the conditions of this study, dinocap did not significantly affect hematology, clinical chemistry parameters, and cholinesterase activity of plasma, RBC or brain at 15 and 60 ppm. Due to poor conditions of the high dose animals the certain clinical chemistry parameters such as albumin and globulin levels were affected.

The NOAEL for systemic toxicity is 15 ppm (0.375 mg/kg/day); the LOAEL is 60 ppm (1.5 *mg/kg/day) based on ophthalmoscopic changes and histologic retinal atrophy.*

This chronic feeding study in dogs **is classified as Acceptable/guideline and satisfies the guideline data requirement for a chronic toxicity study (83-1b) in dogs.**

Dose and Endpoints for Risk Assessment: The Systemic Toxicity NOAEL = 0.375 mg/kg/day and LOAEL = 1.5 mg/kg/day in male dogs, based on **ophthalmoscopic changes and histologic retinal atrophy.**

Uncertainty Factor(s): An uncertainty factor of 100 is proposed to account for inter-species extrapolation (10X) and intra-species variability (10X).

Comments about Study/Endpoint/Uncertainty Factor(s): The endpoint was selected from the chronic dog study because dogs appear to be more sensitive species than rats or mice. Although this dog chronic study was conducted with dinocap with 78% a.i., the endpoint was selected from this because no dog chronic study is available with new formulation (92% a.i.).

Chronic RfD = $\frac{0.375 \text{ mg/kg/day (NOAEL)}}{100 \text{ (UF)}}$ = 0.00375 **mg/kg/day**

2.3 Occupational / Residential Exposure

2.3.1 and 2.3.2 Short-Term (1-7 days) and Intermediate-Term (7 Days to Several Months) Incidental Oral Exposure

No endpoint selection is required for this exposure period since this chemical is not registered for residential use and incidental oral exposure is not expected to occur.

2.3.3 Dermal Absorption

Study Selected: Dermal Penetration Study in Monkey Guideline #: 85-2

Accession No.: 260614

Executive Summary:

In a dermal penetration study (Accession No. 260614), ^{14}C-ring-labeled dinocap (94% a.i.) was dermally applied to female Rhesus monkeys (4/dose) at the rate of 40 (group 2a:water-wash), 40 (group 2b:ethanol-wash) and 2500 (group 3:ethanol-wash) ug/cm^2 for 6 hours. The application area was 40, 40 and 0.64 cm^2 for groups 2a, 2b and 3, respectively. Six hours after dermal exposure, the application site was washed with water saturated cotton balls (group 2a) or ethanol laden cotton balls followed by water laden cotton balls (groups 2b and 3).

The recovery of radioactivity in 4 days following 6 hours exposure to 40 (water-wash), 40 (ethanol-wash), and 2500 (group 3:ethanol-wash) ug/cm^2 was 10.3, 5.1, and 2.6% of the applied dose in urine and 3.9, 7.3, and 1.6% of the dose in feces, respectively.

The recovery of radioactivity in dermal wash samples after 6 hours exposure to 40 (water-wash), 40 (ethanol-wash), and 2500 (group 3:ethanol-wash) ug/cm^2 was 17.5, 40.7, and 75.2% of the applied dose, respectively. The recovery data indicated that the use of ethanol as washing solution (groups 2b and 3) apparently was more effective in removing the test chemical from the application site than water.

Total recovery of radioactivity in dermal wash samples and excreta (urine and feces) in 4 days following 6 hours exposure to 40 (water-wash), 40 (ethanol-wash), and 2500 (group 3:ethanol-wash) ug/cm^2 was 49.28, 71.72, and 84.94% of the applied dose, respectively. [Note: Some radiolabel may still be retained at the original application site. However, amounts of dose remained on the skin were not measured.]

An additional excretion study of dinocap in four monkeys was conducted after a single intravenous administration of ^{14}C-ring-labeled dinocap at 0.2 mg/kg. The recovery of radioactivity in the urine and feces were 49.2 and 35.3% of the injected dose in 4 days, respectively.

Dermal absorption of dinocap in 4 days following 6 hours exposure to 40 (water-wash group), 40 (ethanol-wash group) and 2500 ug/cm^2 (ethanol-wash group) was **42.4, 20.9, and 10.6**% of the applied dose, respectively, using the following equation:

$$\text{Dermal absorption} = \frac{^{14}\text{C urinary excretion (dermal)}}{^{14}\text{C urinary excretion (i.v.)}} \times 100$$

This study is classified as acceptable/guideline and satisfies the guideline data requirement for a dermal penetration study (85-2) in monkeys.

Dermal Absorption Factor: **42.4%** in 4 days following 6 hours exposure. Washing skin with water is normally done. Ethanol washing may not be appropriate in the field situation. Therefore, water wash group is preferred over ethanol wash groups.

Comments about Dermal Absorption:

From the above monkey dermal absorption study, HIARC selected 4 day excretion data instead of one day excretion data because the experimental approach utilized to determine dermal absorption preclude estimation of dermal absorption after one day. Estimation of dermal absorption using 4 day excretion data reflect proper correction for urinary excretion of dinocap following i.v. dosing.

There is a dermal penetration study (Accession No. 259639) in rabbits. This study showed that dermal absorption of dinocap (expressed as % of applied dose) in 4 days following 6 hours exposure to ^{14}C-dinocap at 25, 100, and 220 mg/kg varied from 3.8% (applied neat at 25 mg/kg) to 9.2% (wettable dust formulation at 25 mg/kg). This study would be useful when considering the possible exposure to the wettable dust formulation.

Because the permeability characteristics of monkey skin are closer to human than the rabbit, the monkey dermal absorption data is preferred over rabbit data.

2.3.4 Short-Term Dermal (1 - 7 days) Exposure

Study Selected: Developmental Toxicity Study in Mice Guideline **#:** 83-3(a)

MRID No.: 41313001

Executive Summary: See Acute Dietary.

Dose and Endpoint for Risk Assessment: **The NOAEL for developmental toxicity is 4 mg/kg/day; the LOAEL is 10 mg/kg/day based on the** slight (non-significant) increase in

incidences of cleft palate and eyelids-open relative to the controls.

Comments about Study/Endpoint: Although a dermal developmental toxicity study in mice is available, the HIARC selected the oral study in mice because of the concern for the developmental effects seen at lower doses, via the oral route in two studies (LOAEL = 10 mg/kg/day; < 5 mg/kg/day) compared to the dermal study (LOAEL = 100 mg/kg/day).

In addition, the endpoint was selected from the mouse developmental toxicity study because mice appear to be more sensitive species than rats or rabbits.

Also, the endpoint selection from mouse developmental toxicity is supported by a dermal developmental study in rabbits (ACCESSION Nos. 256934 and 259645). In this study, dinocap (87.8% a.i.) was dermally applied at concentrations of 0, 25, 50, or 100 mg/kg/day to presumed pregnant New Zealand white rabbits (18/dose) on gestation days (GDs) 7 through 19. Does were sacrificed on GD 29. The NOAEL for maternal toxicity is 50 mg/kg/day; the LOAEL is 100 mg/kg/day based on decreased body weights and food consumption. The NOAEL for developmental toxicity is 50 mg/kg/day; the LOAEL is 100 mg/kg/day based on increased litter and fetal incidences of skull bone islands and accessory skull bones and decreased fetal weight.

2.3.5 Intermediate-Term Dermal (1-Week to Several Months) Exposure

Study Selected: Mouse developmental toxicity study Guideline #: 83-3 (a)

MRID No.: 41313001

Executive Summary: See Short term.

Dose and Endpoint for Risk Assessment: The NOAEL for developmental toxicity is 4 mg/kg/day; the LOAEL is 10 mg/kg/day based on the slight (non-significant) increase in incidences of cleft palate and eyelids-open relative to the controls.

Comments about Study/Endpoint: See short term.

2.3.6 Long-Term Dermal (Several Months to Lifetime) Exposure

Study Selected: Chronic Feeding Study - Dog Guideline #: 83-1b

Accession No.: 247957

Executive Summary: see Chronic Dietary

Dose and Endpoint for Risk Assessment:

The Systemic Toxicity NOAEL = 0.375 mg/kg/day and LOAEL = 1.5 mg/kg/day in male

dogs, based on **ophthalmoscopic changes and histologic retinal atrophy.**

Comments about Study/Endpoint:

This dose/endpoint was also used to derive the chronic RfD.

2.3.7 Inhalation Exposure (All Duration)

Except for an acute inhalation toxicity study, the results of which place DINOCAP in Toxicity Category III (LC_{50} = 0.9 mg/L), **no other studies are available via this route**. Therefore, the HIARC selected the oral NOAELs of 4 mg/kg/day from developmental toxicity study in mice for Short-Term and Intermediate-Term inhalation risk assessments. For Long-term risk assessment, the HIARC selected the oral NOAEL of 0.375 mg/kg/day from the chronic feeding study in dogs. Since an oral value is selected, route-to-route extrapolation should be as follows.

When route-to-route extrapolations is recommended: 1) **convert** the inhalation exposure (μg/lb a.i) and the dermal exposure (mg/lb a.i) to oral equivalent doses (mg/kg); 2) **combine** the converted oral equivalent doses to get a combined dose for total (dermal + inhalation) exposure; and 3) this combined dose should then be **compared** with the oral NOAEL to calculate the Margins of Exposure.

2.3.8 Margins of Exposures for Occupational/Residential Risk Assessments

A MOE of 100 is adequate for occupational exposure and the MOEs for residential (dermal and inhalation) exposure are 1000 as determined during risk characterization by the FQPA Safety Factor Committee.

2.4 Recommendation for Aggregate Exposure Risk Assessments

For acute aggregate exposure risk assessment, combine the high end exposure values from food + water and compare it to the acute RfD.

For short-, intermediate-, and long-term aggregate exposure risk assessment, combine the average values from food + water together with short or intermediate dermal (corrected for %DA) + short or intermediate inhalation (corrected for %IA) exposure and compared to the oral NOAEL (oral equivalent doses were selected for dermal and inhalation exposures).

3. CLASSIFICATION OF CARCINOGENIC POTENTIAL

The HED RfD/ Peer Review Committee (HED Doc. No. 011076 dated June 24, 1994) considered that the carcinogenicity phase of the rat study (MRID No. 41065401 and ACCESSION No.

00247959) and the carcinogenicity study in mice (MRID Nos. 418639801, 42079102) were considered to be adequate. The high dose levels tested in both rats and mice were considered to be adequate for carcinogenicity testing. The treatment did not alter the spontaneous tumor profile in either animal species. In accordance with the 1986 Cancer Risk Assessment Guideline, dinocap is placed in **"Group E"**; non-carcinogenic to humans.

4. MUTAGENICITY

Dinocap was negative for inducing mutations in all acceptable guideline studies of the standard battery of mutagenicity tests except for Ames studies. In Ames studies, dinocap was weakly positive at best and limited to high doses. These studies satisfy mutagenicity testing requirements.

5. FQPA CONSIDERATIONS

The Health Effects Division (HED) FQPA Safety Factor Committee met on March 13, 2000 to evaluate the hazard and exposure data for dinocap and recommended that the FQPA safety factor (as required by the Food Quality Protection Act of August 3, 1996) be retained at 10x when assessing the risks posed from the use of this pesticide (HED DOC. NO. 014071).

6. HAZARD CHARACTERIZATION

The toxicity data indicate that dinocap has low acute oral, dermal and inhalation toxicity. It is a skin sensitizer. It causes moderate eye and skin irritation. The chronic feeding toxicity study in rats demonstrated that dinocap induced liver toxicity (increased relative liver weights and slight to moderate panlobular hepatocellular hypertrophy) and thyroid toxicity (increased incidences of thyroid follicular cell hypertrophy and altered colloid). The chronic feeding toxicity study in dogs demonstrated that dinocap induced ophthalmoscopic changes and histologic retinal atrophy. The carcinogenicity data showed that carcinogenic potential was not exhibited by dinocap in rats and mice.

Dinocap produced developmental toxicity in mice and rabbits and it did not affect reproductive parameters in rats. Dinocap was negative for inducing mutations in all acceptable guideline studies of the standard battery of mutagenicity tests except for Ames studies. In Ames studies, dinocap was weakly positive at best and limited to high doses.

Dermal absorption studies showed that dermal absorption of dinocap (expressed as % of applied dose) in 4 days following 6 hours exposure to ^{14}C-dinocap was 42.4% and 9.2% in monkeys and rabbits, respectively.

There is high confidence in the chronic RfD of 0.00375 mg/kg/day. This was based on the NOAEL of 0.375 mg/kg/day from the chronic study in dog and uncertainty factor of 100. The LOAEL for 1.5 mg/kg/day in male dogs was based on **ophthalmoscopic changes and histologic retinal atrophy.**

The database is adequate to evaluate FQPA assessment and consists of developmental studies in the mice and rabbits, and a two generation reproduction study in the rats. Based on the findings in the developmental toxicity study in mice and rabbits, there appears to be an increased severity of effects noted in the offspring at maternally toxic doses. In addition, neurotoxicity in the form of clinical signs [such as swimming behavior abnormalities characterized by torticollis condition consistent with malformation of the inner ear (absence of otoliths)] was observed in the developmental toxicity study in rats. Also, ophthalmoscopic changes and histologic retinal atrophy was observed in the chronic study in dogs. In addition, a 30-month chronic/carcinogenicity study in rat (1980 study) showed an increased incidence of degeneration/atrophy of the calf muscle in the mid and high dose (10 and 100 mg/kg/day) females and degeneration/atrophy of the sciatic nerve in the high dose (100 mg/kg/day) males and females (MRID No. 41065401; Accession No. 247959).

7. DATA GAPS

Acute and subchronic neurotoxicity studies in rats and a developmental neurotoxicity study in rats have been recommended by the HIARC. In addition, due to the potential of long-term inhalation exposure the HIARC recommended a 90-day inhalation toxicity study in rats to address the concerns for assessing risks posed to workers (greenhouse use) by this route.

8 ACUTE TOXICITY

Acute Toxicity of Dinocap

Guideline No.	Study Type	MRID No.	RESULTS	TOXICITY CATEGORY
870.1100	Acute Oral - Rat	42124301	LD 50 = > 500 and 5,000 mg/kg (both sexes)	III
870.1200	Acute Dermal - Rabbit	42124302	LD50 => 5,000 mg/kg	IV
870.1300	Acute Inhalation - Rat	42124303	LC50= 0.9 mg/L	III
870.2400	Eye Irritation- Rabbit	42124304	moderate irritation; Corneal and conjunctival effects at 24 hours; corneal effects cleared by day 2 and conjunctival effects cleared by day 7.	III
870.2500	Dermal Irritation- Rabbit	42124305	moderate irritation at day 3 and cleared by day 14.	III
870.2600	Dermal sensitization - Guinea pig	42124306	a sensitizer	N/A

9 SUMMARY OF TOXICOLOGY ENDPOINT SELECTION

The doses and toxicological endpoints selected for various exposure scenarios are summarized below.

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary (Female 13+)	NOAEL=4	slight (non-significant) increase in incidences of cleft palate and eyelids-open	Developmental–mouse
	UF=100	**Acute RfD = 0.04 mg/kg/day**	
Acute Dietary (General population)	An appropriate endpoint attributable to a single dose was not identified.		
Chronic Dietary	NOAEL=0.375	ophthalmoscopic changes and histologic retinal atrophy	Chronic feeding –dog
	UF=100	**Chronic =0.00375 mg/kg/day**	
Incidental Oral, Short- and Intermediate-Term	No endpoint selection is required for this exposure period since this chemical is not registered for residential use and incidental oral exposure is not expected to occur.		
Short-Term [a] (Dermal)	oral NOAEL=4	slight (non-significant) increase in incidences of cleft palate and eyelids-open	Developmental–mouse
Intermediate-Term (Dermal)	oral NOAEL=4	**slight (non-significant) increase in incidences of cleft palate and eyelids-open**	**Developmental–mouse**
Long-Term (Dermal)	**oral NOAEL=0.375**	**ophthalmoscopic changes and histologic retinal atrophy**	**Chronic feeding –dog**
Inhalation (short & intermediate) [b]	**oral NOAEL=4**	**slight (non-significant) increase in incidences of cleft palate and eyelids-open**	**Developmental–mouse**
Inhalation (long)	**oral NOAEL=0.375**	**ophthalmoscopic changes and histologic retinal atrophy**	**Chronic feeding –dog**

a = Since an oral NOAEL was selected, a dermal absorption factor of 42% should be used in route-to-route extrapolation.

b = Since an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) should be used in route-to-route extrapolation.

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Chemical:	**Dinocap**
PC Code:	**036001**
HED File Code	**21100 HIARC**
Memo Date:	**02/08/2001**
File ID:	**TX014466**
Accession Number:	**412-02-0006**

HED Records Reference Center
12/04/2001