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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 29-November-99

SUBJECT: **Occupational Exposure and Risk Assessment/Characterization for Chlorfenapyr use in Greenhouses and Shadehouses. PC Code: 129093. DP Barcode: D241749.**

FROM: Dana Vogel, Chemist
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TO: Ann Sibold/Arnold Layne
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THRU: Olga Odiott, Biologist
RAB1/HED

Melba Morrow, Branch Senior Scientist 11/29/99
RAB1/HED

The Registration Division has requested that HED assess the potential occupational exposure resulting from the greenhouse/shadehouse use of chlorfenapyr on non-edible ornamentals. This document provides such an assessment. The risk estimates are based on toxicological endpoints identified in HED's Toxicology Endpoint Selection (TES) Document dated 11/17/97 (Attachment 1) and the Hazard Identification Assessment Review Committee (HIARC) document dated 11/18/99 (Attachment 2). Table 1.0 summarizes the endpoints used in this risk assessment.

Table 1. Chlorfenapyr Toxicological Endpoints - Occupational Exposure Risk Assessment for the Greenhouse Use

EXPOSURE SCENARIO	DOSE	ENDPOINT	STUDY
Short-Term (dermal)	NOAEL=100 mg/kg/day (dermal study)	LOAEL=400 mg/kg/day (increased cholesterol, relative liver weights and cytoplasmic vacuolation of the liver in male and females	28-day dermal toxicity study - rabbits

Intermediate-Term (dermal)	NOAEL: 100 mg/kg/day (dermal study)	LOAEL=400 mg/kg/day (increased cholesterol, relative liver weights and cytoplasmic vacuolation of the liver in male and females	28-day dermal toxicity study - rabbits
Long-Term (dermal)	NOAEL=2.6 mg/kg/day[1] (oral study)	LOAEL = 13.6 mg/kg/day (decreased body weight gains brain lesions (vacuolation) and/or scabbing of the skin in a 1 year neurotoxicity study in rats and a chronic/carcinogenicity study in mice) Acceptable MOE = 100	1 yr neurotox. study - rats (oral), chr/ onco - mice
Short-Term (inhalation)	NOAEL=4.2 mg/kg/day[2] (oral study)	LOAEL = 6.1 mg/kg/day (reduced body weight gain and feed efficiency and emaciation)	Subchronic oral study-dog
Intermediate- Term (inhalation)	NOAEL=4.2 mg/kg/day[2] (oral study)	LOAEL = 6.1 mg/kg/day (reduced body weight gain and feed efficiency and emaciation)	Subchronic oral study-dog
Long-Term (inhalation)	NOAEL=2.6 mg/kg/day[2] (oral study)	LOAEL = 13.6 mg/kg/day (decreased body weight gains, brain lesions (vacuolation) and/or scabbing of the skin in a 1 year neurotoxicity study in rats and a chronic/ carcinogenicity study in mice)	1 yr neurotox. study - rats (oral), chr/ .onco - mice

[1] Use the appropriate dermal absorption factor (5 %) since the NOAEL is from an oral study.
[2] Use the appropriate inhalation absorption factor (100 %) since the NOAEL is from an oral study.

Summary of Use Patterns and Formulations

Chlorfenapyr is an active ingredient developed by American Cyanamid corporation as a foliar miticide-insecticide to control spider mites, worm pests, and thrips. American Cyanamid is seeking registration for use on non-edible ornamentals crops grown in greenhouses and shadehouses. Currently, there are no registered uses of chlorfenapyr that result in residential exposures.

Pylon is a liquid formulation containing 21.4% of the active ingredient chlorfenapyr. The label recommends that applications be made pre-bloom at 5 to 7 day intervals. For best results, thorough foliar coverage applications should be made at the first signs of pests, prior to crop damage. For resistance management purposes, the label recommends against more than 2 or 3 sequential applications per growing cycle, dependent upon the situation. As specified on the proposed label, the maximum application rate (AR) is **0.64 lbs ai** (41 oz. of product)/acre, for periods of heavy pest infestations.

Occupational Exposure and Risk Assessment/Characterization

Since it is assumed that a greenhouse worker will treat a variety of ornamentals on a year-round basis. short-. intermediate-, and long-term exposures are possible from the proposed use. The Cancer Peer Review Committee (CPRC) characterized chlorfenapyr as a "cannot be determined, suggestive" carcinogen, based on increases in tumors in the rat only, which were not considered

to be persuasive but could not be dismissed (CPRC, 9/25/96). A Q_1* has not been established. The HIARC (11/99) did not recommend that a cancer assessment be done at this time. The HIARC memorandum, dated 11/18/99, will be amended to reflect this change.

Handler Exposures and Assumptions

Table 1.1 lists the assumptions used in the handler exposure assessment.

Table 1.1 Assumptions for Worker Exposure Assessments using High Pressure Handwand Equipment

Handler & Application equipment [1]	Unit Exposure mg/lb ai		Application Rate (AR) lb ai/ A	Acres Treated [2]	Data Sources
	Dermal	Inhalation			
M/L/A	2.5	0.12	0.64	2	Unit Exposure: Pesticide Handlers Exposure Database V1.1, Surrogate Exposure guide, May 1997: mixer/loader/applicator files (liquid, open pour; high pressure hand wand). low confidence data. Acres treated based on: Stamper, J.H. et al (1989) Pesticide exposure to greenhouse handgunners. Arch Environ Contam Toxicol 18: 515-529.

1 -High Pressure Hand Wand; handlers wearing long sleeved shirts, long pants, and gloves
2 -150 m X 40 m commercial greenhouse

Handler Exposure and Risk Assessment

Table 1.2 summarizes the exposure and risk estimates for mixer/loaders and applicators from the proposed greenhouse uses for chlorfenapyr. The mixer/loader/applicator using a high pressure handwand is expected to represent the scenario with the highest potential exposure. Exposure estimates were calculated using the assumptions listed in Table 1.1.

Table 1.2 Occupational Exposure and Risk Estimates

Exposure Scenario	Average Daily Dose (mg/kg/day)	Short-/Intermediate-term MOEs[1]	Long-term MOE [2]
Mixer/ Loader/Applicator	0.046-dermal	2200-dermal	580
	0.0022-inhalation	1900-inhalation	

Average Daily Dose (ADD) = unit exposures X application rate X acres/day X 1/70 kg bw
MOE = NOAEL/ADD; The level of concern is for MOEs below 100.
Dermal NOAELs = for short and intermediate-term = 100 mg/kg/day; for long-term = 2.6 mg/kg/day **(long-term dermal exposure is corrected for 5% dermal absorption)**
Inhalation NOAELs = for short and intermediate-term = 4.2 mg/kg/day; for long-term = 2.6 mg/kg/day **(all inhalation exposure assumes 100% absorption)**
[1] The endpoint selected for the short- and intermediate-term assessments is based on a 28-day dermal toxicity study in rabbits. This dosing duration is expected to adequately represent the potential intermediate-term exposures.
[2] Long-term MOE = 2.6 mg/kg/day/Total Exposure (dermal + inhalation)

All calculated MOEs for chlorfenapyr are greater than 580. Therefore, worker potential risks from exposures to chlorfenapyr do not exceed the HED's level of concern.

Post-Application Exposures and Assumptions

There are potential post-application exposures to workers entering treated areas for routine crop maintenance tasks such as irrigating, sorting, and packing treated ornamental plants. Since Pylon™ is used pre-bloom on ornamental plants (African violets, azaleas, pansy, vinca and the like), exposure from high dermal transfer activities such as cutting or pruning flowers is not expected. The majority of exposure is expected from sorting and packing of ornamental plants. Irrigation activities are also a possibility, (although most commercial greenhouses have mechanized irrigation systems). The activity representing the highest potential dermal post-application exposure for the proposed use of chlorfenapyr is irrigation, with a transfer coefficient (TC) of 4,000 cm^2/hour. Therefore, the assessment is based on the irrigation post-application activity in order to represent a high-end scenario.

There are no chemical-specific post-application exposure data available to determine the potential risks to workers from the proposed greenhouse uses. Despite the lack of data, and in order to provide an estimate of the potential risks associated with the exposure scenarios being considered, a risk assessment was conducted using the following assumptions: application rate of 0.64 lb ai/A, 20% of the application rate available as dislodgeable residues available on day 0, a TC of 4,000 cm^2/hour (generic value, based on the Transfer Coefficients Surrogate Table developed by the HED Exposure SAC), and a work day of 8 hours.

Since the label specifies that an applications interval of 5-7 days, higher dislodgeable residues are expected for the short- and intermediate-term exposures. Therefore, day 0 residues were used to calculate short- and intermediate-term exposures for the proposed greenhouse use of chlorfenapyr. For long-term exposures, workers are expected to be exposed to dissipated residues. Therefore, long-term post-application exposures were calculated using an average of DFRs available from day 1 through day 5.

Post-Application Exposure and Risk Assessment

Table 1.3 summarizes the post-application exposure estimates for the proposed use of chlorfenapyr.

Table 1.3 Post-application Exposure and Risk Assessments

Exposure Scenario	Exposure duration	Transfer Coefficient (cm^2/hr)	Dislodgeable residues (ug/cm^2)	Average Daily Dose (mg/kg/day)	MOE
Irrigation of ornamental plants AR = 0.64 lb ai/A	Short/Intermediate-term	4,000	1.4 (DFR on day 0)	0.66[1]	150
	Long-term		1.1 (average DFR day 1-5)	0.025[2]	100

1-Using DFRs available on day 0
2-Using an average DFR from days 1-5
Surrogate Dislodgeable residue (DFR) = application rate X % available as dislodgeable residue X 4.54E8 ug/lb X 2.47E-8 A/cm^2
Application rate = 0.64 lb ai/A (product label); 20% available as dislodgeable residue on day 0 and 10 % dissipation/day
ADD =DFR (ug/cm^2) X TC (cm^2/hr) X hrs/day X 0.001 mg/ug X 1/ BW ; BW= 70kg for adults;
MOE = NOAEL/ ADD; for short and intermediate-term NOAEL = 100 mg/kg/day; for long-term NOAEL = 2.6 mg/kg/day **(long-term dermal exposure is corrected for 5% dermal absorption)**
The level of concern is for MOEs below 100.

These estimates indicate that potential exposure to workers from chlorfenapyr do not exceed the HED's level of concern for the proposed ornamental use in greenhouses and shadehouses. It should be noted that these estimates do not take into account the resistance management practices specified on the label (such as no more than 2 to 3 consecutive applications). The label suggests alternating chlorfenapyr treatments with other miticide/insectides to avoid developing pest resistance to this product. Additionally, this assessment assumes an 8 hour work day which is likely to be a high number of hours per day for irrigation activities. For these reasons, this assessment is considered to be high-end.

Restricted Entry Interval (REI)

The proposed interim REI is 12 hours based on chlorfenapyr's acute toxicity classification of III for eye irritation, and the dermal and inhalation routes of exposure.

cc (with attachments): Chemical file, D. Vogel (RAB1), O.Odiott (RAB1)
RDI: O.Odiott (11/29/99), M. Morrow (11/29/99)
D.Vogel:809B:CM#2:(703)305-0874:7509C:RAB1

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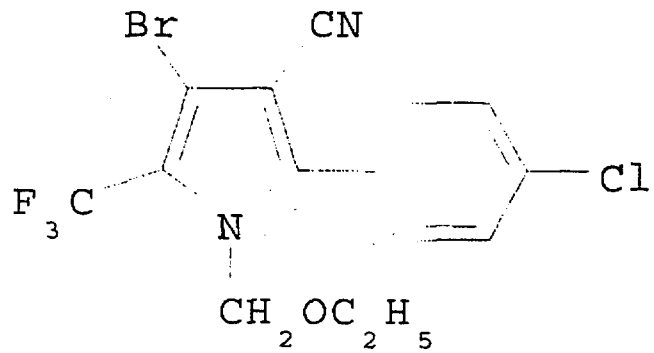
ATTACHMENT 1 - Toxilogical Endpoint Selection Document, 11/17/97
(Available Electronically)

TOXICOLOGY ENDPOINT SELECTION DOCUMENT
SECOND REVISION 11/17/97

Chemical Name: Pirate®

PC Code: 129093

Structure



The Health Effects Division Toxicology Endpoint Selection Committee considered the available toxicology data for Chlorfenapyr (Pirate®) at a meeting held on July 23, 1996 . 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. *This is a second revision of the original TES document on Pirate® (report date 7/24/96):there is no change in the endpoints selected for use in risk assessment including the RfD and the uncertainty factors used, however there is a modification in which studies are used to support the chronic dermal and chronic dietary exposure scenarios. This document also includes the call made by the Cancer Peer Review Committee. This document supersedes the previous Toxicology Endpoint Selection Document (7/24/96)and the first revision (1/27/97).*

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.

Toxicologist: Marion Copley Date: 11/17/97

Branch Senior Scientist (RAB1): Melba Morrow Date: 11/17/97

Chair, Hazard ID Committee: Clark Swentzel Date: 11/21/97

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DERMAL ABSORPTION DATA: A dermal absorption study was not available. Therefore, a dermal absorption value of 5% was calculated based on the route-to-route extrapolation using the maternal NOEL of 5 mg/kg/day from the developmental toxicity study in rabbits and the systemic NOEL of 100 mg/kg/day from the 28-day dermal toxicity study in rabbits. This dermal absorption value will be used ONLY for the chronic exposure risk assessment since an oral study was selected for this scenario. Dermal absorption factor is not needed for the short-and intermediate-term exposure risk assessments since a 21-day dermal toxicity was used for these scenarios.

MRID: 42770222 and 43492831

% absorbed: 5%

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ACUTE DIETARY ENDPOINT (ONE DAY)

Study Selected - Guideline No.: Acute neurotoxicity study - rats §81-8
MRID No.:43492829

Summary: In an acute neurotoxicity study, AC 303,630, (94.5% ai, Lot No. AC 7504-59-A) was dissolved in 0.5% carboxymethylcellulose and administered once, via gastric intubation in a dosing volume of 10 ml/kg/dose, to 60 Sprague-Dawley CD rats (10/sex/group) at dose levels of 0, 45, 90, and 180 mg/kg. All rats were observed for 2 weeks following dosing. The rats were evaluated for reactions in functional observational and motor activity measurements pretest and on study days 1, 8, and 15. In addition, five rats per group were examined for neuropathologic lesions.

Two males and two females in the 180 mg/kg dose group died within 7 hours of dosing, possibly as a result of accidental injury during treatment. Surviving rats in this dose group exhibited changes in gait, locomotion, and arousal, and 20-30% of the males and females were lethargic on the day of treatment. In the 90 mg/kg dose group, 20% of the males were lethargic on the day of treatment. No dose-related effects on body weights, food consumption, neurobehavioral observations, or gross or histological post mortem examinations were noted. **The LOEL is 90 mg/kg, based on lethargy of the rats on the day of treatment. The NOEL is 45 mg/kg.**

This acute neurotoxicity study is **Supplemental**, but can be upgraded to acceptable if adequate historical control FOB data are provided.

Dose and Endpoint for use in risk assessment: NOEL = 45 mg/kg/day based on lethargy exhibited by rats at the 90 mg/kg/day (LOEL) on the day of treatment.

Comments about study and/or endpoint: None

This risk assessment is required. An Uncertainty Factor (UF) of 100 and 10-fold modifying factor (MF) is appropriate.

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SHORT TERM OCCUPATIONAL OR RESIDENTIAL EXPOSURE (1 TO 7 DAYS)

DERMAL EXPOSURE:

Study Selected - Guideline No.: 28-day dermal toxicity study - rabbit §82-2

MRID No.: 43492831

Summary: In a repeated dose dermal toxicity study, AC 303,630 (Pirate; 94.5% a.i., Lot No. AC 7504-59A) was applied to the shaved skin of six New Zealand White rabbits/sex/dose at dose levels of 0, 100, 400, or 1000 mg/kg, 6 hours/day, 5 days/week for 4 weeks.

Rabbits of both sexes in the 400 and 1000 mg/kg treatment groups exhibited statistically significant and concentration-related increases in serum cholesterol (60-95%) and relative liver weights (22-43%), and suffered from cytoplasmic vacuolation of the liver. The vacuolation of the liver was minimal to slight for male and female rabbits in the 400 mg/kg treatment groups (4 of 12 animals), and minimal to moderately severe for the 1000 mg/kg treatment groups (8 of 11 animals). In addition, female rabbits in the 1000 mg/kg treatment group exhibited a 97% increase in serum alanine aminotransferase ($p < 0.05$) concentrations. No differences were observed between rabbits in the 100 ppm treatment groups and the control groups. **The LOEL is 400 mg/kg for both sexes, based on changes in liver chemistry and morphology. The NOEL is 100 mg/kg.**

This subchronic toxicity study is classified **acceptable** and does satisfy the guideline requirement for a repeated dose dermal toxicity study (§82-2) in rabbits.

Dose and Endpoint for use in risk assessment: NOEL = 100 mg/kg/day based on increases in cholesterol and relative liver weights and histological lesions in the liver of both sexes of rabbits at 400 mg/kg/day (LOEL).

Comments about study and/or endpoint: None

This risk assessment is required. An Uncertainty Factor (UF) of 100 and 10-fold modifying factor (MF) is appropriate.

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INTERMEDIATE TERM OCCUPATIONAL OR RESIDENTIAL EXPOSURE (1 WEEK TO SEVERAL MONTHS)

DERMAL EXPOSURE:

Study Selected - Guideline No.: 28-day dermal toxicity study - rabbit §82-2

MRID No.: 43492831

Summary: See **Short Time Exposure.**

Dose and Endpoint for use in risk assessment: NOEL = 100 mg/kg/day based on increases in cholesterol and relative liver weights and histopathological lesions in the liver of both sexes of rabbits at 400 mg/kg/day (LOEL).

Comments about study and/or endpoint:

This risk assessment is required. An Uncertainty Factor (UF) of 100 and 10-fold modifying factor (MF) is appropriate.

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CHRONIC OCCUPATIONAL OR RESIDENTIAL EXPOSURE (SEVERAL MONTHS TO LIFETIME)

DERMAL EXPOSURE:

Two Studies Selected -

1) Guideline No.: One Year Neurotoxicity study - rats §82-7
MRID No.: 43492833

Summary: In a one-year dietary neurotoxicity study[1] (MRID 43492833), AC 303,630 (Pirate; 94.5% ai, Lot No. AC 7504-59-A) was administered in the diet at 0, 60, 300, or 600 ppm (52-week average 0, 2.6, 13.6, or 28.2 mg/kg/day, respectively, for males; 0, 3.4, 18.0, or 37.4 mg/kg/day, respectively, for females) to Sprague-Dawley CD BR VAF/Plus rats (25/sex/group) for 52 weeks, followed by a 16-week recovery period during which the remaining rats were fed the control diet. The rats were evaluated for reactions in functional observational battery followed by motor activity measurements 1 week before the test diets were provided; 4, 8, 13, 26, 39, and 52 weeks after the first day of exposure; and 13 weeks after the cessation of treatment. A portion of the rats in each treatment group were sacrificed for neuropathological examination following 13 or 52 of exposure, or 16 weeks of recovery.

In the 600 ppm dose group, both sexes exhibited statistically significant decreases in average body weights, body weight gains, absolute and relative feed consumption, feed efficiency, and water consumption (males only). Neurohistological examination of males sacrificed after 13 weeks of exposure revealed myelin sheath swelling in the spinal nerve roots (5/5), compared to 2/5 in the controls. At 52 weeks, a more generalized myelinopathic process consisting of vacuolar myelinopathy (6/10), vacuolation (6/10), and/or mild myelin sheath swelling (9/10), was found. This process was not associated with myelin or axon degeneration and was not evident in rats sacrificed after 16 weeks of recovery. In the 300 ppm dose group, both sexes exhibited decreases in average body weights, body weight gains, feed efficiency, absolute feed consumption (females only) and water consumption (males only) at various times during the exposure period and body weight gains were reduced (non-significantly) for males during recovery. The myelinopathic observations described in the 600 ppm group males was also found in the 300 ppm group of rats after 13 and 52 weeks exposure but were less severe and at a lower incidence. In the 60 ppm dose group rats, minimum myelin sheath swelling was seen in the Gasserian ganglia of one male at 52 weeks and spinal nerve roots of 3/5 males (compared to 2/5 controls) after 13 weeks of exposure. The toxicologic importance of these findings is equivocal since swelling in the spinal nerve roots was absent in the 60 ppm group after 52 weeks. Neuropathological changes were confined to males; females were not affected. **The LOEL is 300 ppm (13.6 mg/kg/day) based on the presence of myelinopathic alterations in the 300 ppm group male rats, decreased average body weights, body weight gains, feed**

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[1] Although, the sponsor put 83-1a on the cover of the study, the study only satisfies the 82-7SS requirement and was not meant to be a chronic rat study.

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efficiency, absolute feed consumption (females) and water consumption (males). The NOEL is 60 ppm (2.6 mg/kg/day).

This one-year dietary neurotoxicity study is classified **Acceptable** and satisfies the guideline requirement for a neurotoxicity study (82-7SS) in rats.

2) Guideline No.: Combined chronic toxicity/oncogenicity study - mice §83-5
MRID No.: 43492838

Summary: In a chronic toxicity/oncogenicity study, Pirate (94.5% a.i., Lot No. AC-7504-59A) was administered to 65 male and 65 female Swiss Crl:CD-1(ICR)BR mice/sex/dose in the diet at dose levels of 0, 20, 120, or 240 ppm (0, 2.8, 16.6, or 34.5 mg/kg/day, respectively, in males; 0, 3.7, 21.9, or 44.5 mg/kg/day, respectively, in females) for 80 weeks.

Chronic toxicity observed in males and females at 120 and 240 ppm included non-neoplastic brain vacuolation primarily in the white matter of the corpus callosum, tapetum, hippocampus, and cerebellum. The incidence of brain vacuolation in males was 4/65 control, 14/64 mid-, and 49/65 high-dose, and in females it was 10/65 control, 28/65 mid-, and 58/65 high-dose. Males and females at 240 ppm also exhibited vacuolation of the spinal cord and optic nerve. Treatment-related gross pathological changes, including skin ulceration and scabbing, occurred in males and females at the 240 ppm level, and scabbing occurred in males at 120 ppm. **The LOEL for systemic toxicity is 120 ppm (16.6 and 21.9 mg/kg/day in males and females, respectively) based on brain toxicity and scabbing of the skin (males), and the NOEL is 20 ppm (2.8 and 3.7 mg/kg/day for males and females, respectively).**

At the doses tested, there was no treatment-related increase in tumor incidence when compared to controls. The animals may have tolerated a higher dose; however, males and females receiving 240 ppm and females administered 120 ppm exhibited decreased body weight gains of 30% in males and 14% in both female groups. Survival in females was depressed by 40% in the 240 ppm treatment group. Dosing was considered adequate based on decreased body weight gain in males and females.

This chronic/oncogenicity study in mice is **acceptable** for oncogenicity and satisfies the guideline requirement for a carcinogenicity study (83-2) in mice. The study is supplementary for chronic toxicity (83-1) because it is missing clinical chemistry and urinalysis data, and absolute organ weights were measured on only 10 mice/sex/dose at terminal sacrifice.

Dose and Endpoint for use in risk assessment: NOEL = 3 mg/kg/day (rounded from 2.6 and 2.8 mg/kg/day from studies 1 and 2 above, respectively) based on the non-neoplastic brain lesions observed in male rats and both sexes of mice as well as the scabbing of skin in male mice at 16.6 mg/kg/day (LOEL).

Comments about study and/or endpoint: The neurotoxicity study was used to establish the RfD /also supporting this endpoint were similar central nervous system lesions observed in

the mouse carcinogenicity study (NOEL 2.8 mg/kg/day)]. Since these oral studies were selected for a dermal exposure scenario, the dermal absorption factor of 5% must be used in risk assessment.

This risk assessment is required. An Uncertainty Factor (UF) of 100 and 10-fold modifying factor (MF) is appropriate.

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INHALATION EXPOSURE (ANY TIME PERIOD):

Based on the combined LC_{50} of 1.9 mg/L, chlorfenapyr (Pirate) is placed in Tox. Cat. III, indicating low toxicity by this route (MRID No.:42770209). *However, if there is a concern for high exposure via this route, a risk assessment may be required.*

With the exception of the acute inhalation toxicity study, there are no inhalation toxicity studies available for selection of a dose and endpoint for inhalation exposure risk assessment. There an oral NOEL should be used for risk assessment if needed.

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CANCER CLASSIFICATION AND BASIS: *Pirate® was reviewed by the HED Cancer Peer Review Committee because of possible carcinogenicity trends (meeting date 9/25/96). In accordance with the EPA proposed Guidelines for Carcinogenic Risk Assessment (April 10, 1996), chlorfenapyr was characterized as "cannot be determined, suggestive".*

Q_1* = not established

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RfD AND BASIS: The HED RfD Peer Review Committee (July 18, 1996) has established an RfD of 0.03 mg/kg/day, based on rat 1-year neurotoxicity study (NOEL 2.6 mg/kg/day) *[also supporting this endpoint are similar central nervous system lesions observed in the mouse carcinogenicity study (NOEL 2.8 mg/kg/day)]* and applying an Uncertainty Factor (UF) of 100 to account for interspecies and intraspecies variability and additional 10-fold modifying factor (MF) for lack of understanding of the cause, and possible further unknown toxicity with regard to the developing young is considered appropriate for this chemical.

NOEL for critical study: 2.6 mg/kg in male rats

Study Type - Guideline No.: One year neurotoxicity - rat §82-7

MRID: 43492833

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ACUTE TOXICITY ENDPOINTS:

Acute Toxicity of Pirate

Guideline No.	Study Type	MRID #(S).	Results	Toxicity Category
81-1	Acute Oral	42770207/ 42884201	LD_{50} (95% C.I.) = 441 (195 - 832) mg/kg, males LD_{50} (95% C.I.) = 1152 mg/kg, females LD_{50} (95% C.I.) = 626 (274 - 1085) mg/kg, combined	II
81-2	Acute Dermal	42770208	LD_{50} > 2000 mg/kg (Limit Dose)	III
81-3	Acute Inhalation	42770209	LC_{50} (95% C.I.) = 0.83 (0.48 - 1.4) mg/l, (males) LC_{50} (95% C.I.) = > 2.7 mg/l, females) LC_{50} (95% C.I.) = 1.9 (1.1 - 3.3) mg/l, combined	III
81-4	Primary Eye Irritation	42770210	Corneal opacity (4/6), iritis (2/6) and conjunctivitis (6/6) present at 48 hours. At 72 hours iritis was resolved. All rabbits were normal by Day-7.	III
81-5	Primary Skin Irritation	42770211	Non-irritating	IV
81-6	Dermal Sensitization	42770212	Not a skin sensitizer	N/A
81-8	Acute Neurotoxicity	43492829	The LOEL is 90 mg/kg, based on lethargy of the rats on the day of treatment. The NOEL is 45 mg/kg.	Supplementary

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001723

Chemical:	**Chlorfenapyr (proposed common name)**
PC Code:	**129093**
HED File Code	**12000 Exposure Reviews**
Memo Date:	**11/29/99**
File ID:	**DPD241749**
Accession Number:	**412-01-0056**

HED Records Reference Center
12/05/2000