13544

011857

Chemical:	**Pyrethrins**
PC Code:	***069001***
HED File Code	**13000 Tox Reviews**
Memo Date:	***03/12/90***
File ID:	**00000000**
Accession Number:	**412-02-0007**

HED Records Reference Center
12/26/2001

13000

14

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

SRRD/GCSB TRANSMITTAL SHEET FOR PART B's

Pesticide: Pyrethrins I

Transmitted to HED on 1/10/89 Chemical#/Case#: 069001/2580

Chem. Tox.#: 715

Sponsor: Pyrethrin Consortium

CRM: Linda Deluise Phone#: 557-0429

This action contains a request for a DATA WAIVER (X)/

TIME EXTENSION ( ). Label attached: Yes ( )/No ( ) William Dykstra

Branch: Toxicology I-IRS, Section I Reviewer: William Dykstra

Completed: 3/12/90 Concurrence: Karl Baetcke

Response, By Guideline

Guideline #: 81-1 Description: Acute oral/rat

Compliance Codes: Y/1 Data Waiver ( )/Time Extension ( )

MRID No MRID No. Study # Submitted 7/9/86 by CSMA

Discussion: Registrant is required to submit MRID Number or resubmit new complete copy of study.

Recommendation: Review of study could not be located.

Guideline #: 81-2 Description: Acute Dermal/rat

Compliance Codes: Y/4 Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: Registrant will submit new study.

Recommendation: Registratn will submit new study.

Guideline #: 81-3 Description: Acute Inhalation/ rat

Compliance Codes: Y/4 Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: Registrant will submit new study.

Recommendation: Registrant will submit new study.

Guideline #: 81-4 Description: Primary Eye Irritation/rabbit

Compliance Codes: Y/4 Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: Registrant will submit new study.

Recommendation: Registrant will submit new study.

Guideline #: 81-5 Description: Primary dermal irritation/rabbit

Compliance Codes: Y/4 Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: Registrant will submit new study.

Recommendation: Registrant will submit new study.

Guideline #: 81-6 Description: Dermal sensitization/ guinea pig

Compliance Codes: Y/4 Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: Registrant will submit new study.

Recommendation: Registrant will submit new study.

Guideline #: 81-7 Description: Acute delayed neurotoxicity/hen

Compliance Codes: N/ Data Waiver ( )/Time Extension ( )

MRID _____ Study # _____

Discussion: Not required.

Recommendation: Note required.

Guideline #: 82-1(a) Description: 90-day feeding/ rodent

Compliance Codes: Y/3 Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: The registrant is previously committed to supply this study.

Recommendation: The registrant is previously committed to supply this study.

Guideline #: 82-1(b) Description: 90-day feeding/ nonrodent

Compliance Codes: N/7 Data Waiver (X)/Time Extension ( )

MRID None Study # None

Discussion: 90-day dog study will be superseded by 1-year dog study.

Recommendation: The registrant will submit a 1-year dog study in April 1990. 90-day study may be waived if 1-year study is acceptable.

Guideline #: 82-2 Description: 21-day dermal/ rodent/rabbit

Compliance Codes: Y/4 Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: Registrant will submit new study.

Recommendation: Registrant will submit new study.

Guideline #: 82-3 Description: 90-day dermal/ rodent

Compliance Codes: N/ Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: Not required.

Recommendation: Not required.

Guideline #: 82-4 Description: 90-day inhalation/ rodent

Compliance Codes: Y/4 Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: Registrant will submit new study.

Recommendation: Registrant will submit new study.

Guideline #: 82-5(a) Description: 90-day neurotoxicity/ hen

Compliance Codes: N/ Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: Not required.

Recommendation: Not required.

Guideline #: 82-5(b) Description: 90-day neurotoxicity/ mammalian

Compliance Codes: Y/4 Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: Neurotoxicity symptoms were observed in several studies in mammals.

Recommendation: This study is required.

Guideline #: 83-1(a) Description: Chronic feeding/ rodent

Compliance Codes: Y/3 Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: Registrant has previously committed to supply this study.

Recommendation: Registrant has previously committed to supply this study.

Guideline #: 83-1(b) Description: Chronic feeding/ nonrodent

Compliance Codes: Y/3 Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: Registrant has previously committed to supply this study.

Recommendation: Registrant has previously committed to supply this study.

Guideline #: 83-2(a) Description: Oncogenicity/rat

Compliance Codes: Y/3 Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: Registrant has previously committed to supply this study.

Recommendation: Registrant has previously committed to supply this study.

Guideline #: 83-2(b) Description: Oncogenicity/mouse

Compliance Codes: Y/3 Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: Registrant has previously committed to supply this study.

Recommendation: Registrant has previously committed to supply this study.

Guideline #: 83-3(a) Description: Teratogenicity/rat

Compliance Codes: Y/1 Data Waiver ( )/Time Extension ( )

MRID 40288201-02 Study # IRDC #566-002; July 30, 1987

Discussion: NOEL for developmental and maternal effects is greater than 75 mg/kg/day (HDT). Classified supplementary and changed to guideline after review of pilot study used to set dose levels.

Recommendation: Acceptance criteria are fulfilled and DER is recent according to new DER format. A new study is not required.

Guideline #: 83-3(b) Description: Teratogenicity/rabbit.

Compliance Codes: Y/1 Data Waiver ( )/Time Extension ( )

MRID 40288201-03 Study # IRDC #566-004; July 22, 1987

Discussion: Developmental NOEL = 250 mg/kg/day (HDT); maternal NOEL = 25 mg/kg/day. Maternal LEL = 100 mg/kg/ day (decreased weight gain, salivation, arched back). Classified Core-Guideline.

Recommendation: Review is acceptable. Study does not need to be repeated. Acceptance criteria are fulfilled.

Guideline #: 83-3(c) Description: Teratogenicity/mouse

Compliance Codes: / Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: Not required.

Recommendation: Not required.

Guideline #: 83-4 Description: 2-generation reprod./rat

Compliance Codes: Y/3 Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: Registrant has previously committed to supply this study.

Recommendation: Registrant has previously committed to supply this study.

Guideline #: 84-2(a) Description: Gene mutation/

Compliance Codes: Y/4 Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: Registrant will submit new study.

Recommendation: Registrant will submit new study.

Guideline #: 84-2(b) Description: Struct. chrom. aberration

Compliance Codes: Y/4 Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: Registrant will submit new study.

Recommendation: Registrant will submit new study.

Guideline #: 84-2(c) Description: Other genotoxic effects

Compliance Codes: Y/4 Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: Registrant will submit new study.

Recommendation: Registrant will submit new study.

Guideline #: 85-1 Description: General metabolism/rat

Compliance Codes: Y/7 Data Waiver (X)/Time Extension ( )

MRID None Study # None

Discussion: The registrant requests a waiver since natural pyrethrins cannot be radiolabeled in a manner that would facilitate the conduct of a routine rat metabolism study.

Recommendation: Toxicology Branch recommends that the consortium consult with Dr. Iannou on this matter. Study may be required.

Guideline #: 85-2 Description: Dermal Penetration

Compliance Codes: N/ Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: Not required.

Recommendation: Not required.

Guideline #: 86-1 Description: Domestic animal safety

Compliance Codes: N/ Data Waiver ( )/Time Extension ( )

MRID None Study # None

Discussion: Not required.

Recommendation: Not required.

54887:I:Dykstra:HED-8:KENCO:02/27/90:04/02/90:dg:vo:dg:vo:de
R:54922:Dykstra:HED-8:KENCO:03/09/90:04/10/90:CL:sw:vo:ka

DP BARCODE: D155025 REREG CASE # 2580

CASE: 809532 DATA PACKAGE RECORD DATE: 08/30/90
SUBMISSION: S381124 BEAN SHEET Page 1 of 1

* * * CASE/SUBMISSION INFORMATION * * *

CASE TYPE: REREGISTRATION ACTION: PHASE 3 INITIAL SUB
CHEMICAL: 069001 Pyrethrin I
ID#: 069001004713
COMPANY: 004713 PYRETHRUM BOARD OF KENYA
PRODUCT MANAGER: 50 JAY ELLENBERGER 703-308-8085 ROOM: CST 4J1
PM TEAM REVIEWER: LINDA DELUISE 703-308-8066 ROOM: CST 3N3
RECEIVED DATE: 08/30/90 DUE OUT DATE: / /

* * * DATA PACKAGE INFORMATION * * *

DP BARCODE: 155025 EXPEDITE: N DATE SENT: 08/30/90 DATE RET.: / /
DP TYPE: 101 Phase IV Review
ADMIN DUE DATE: 09/20/90 CSF: N LABEL: N

ASSIGNED TO	DATE IN	ASSIGNED TO	DATE IN
DIV : HED	8/31/90	REVR :	/ /
BRAN: TB-HFAS	/ /	CONTR:	/ /
SECT:	/ /		

* * * DATA PACKAGE REVIEW INSTRUCTIONS * * *

For the attached reregistration case, please identify all applicable data requirements and note those for which adaquate data have not been submitted to the Agency
THE PACKAGE CONTAINS 6(a)(2) INFORMATION

ALL REGISTRANTS MEMBER OF CONSORTIUM.

* * * ADDITIONAL DATA PACKAGES FOR THIS SUBMISSION * * *

DP BC	BRANCH	DATE OUT	DUE BACK	INS	CSF	LABEL
155024	EFGB	08/30/90	09/20/90	Y	N	N

EEB
NDEB
DEB

PHASE FOUR REVIEW

(NOTE: This only contains additions and changes from the Phase 2 response.)

Pesticide: Pyrethrin I (Chemical; 069001)

Transmitted to HED on: 8/31/90 Chemical/Case No.: 069001/809532

TOX Chem No.: 715 Sponsor: Several sponsors, such as . . . Pyrethrum Board of Kenya, etc.

CRM: Linda DeLuise Phone No.: (703) 308-8085

Branch: SRRD Reviewer: William Dykstra, Ph.D. William Dykstra 10/12-190

Completed: 9/22/90 Concurrence: Karl P. DeLuise 10/22/90 Roger Gardner 10-19-90

Are there any changes from the reviews in Phase 2? ____ NO X YES (See below)

Response, by Guideline

Guideline No.: 81-1 Acute Oral/Rat

MRID No.: None

Study No.: None

Previously 1986 submitted study or MRID Number for the study will be submitted for Phase 5.

Discussion/Recommendation: Phase 2 could not locate 1986 study.

Guideline No.: 81-2 Acute Dermal/Rabbit

MRID No.: None

Study No.: None

New study will be submitted for Phase 5.

Discussion/Recommendation:

Phase 2 noted that new study will be needed.

Guideline No.: 81-3 Acute Inhalation/Rat

MRID No.: None

Study No.: None

New study will be submitted for Phase 5.

Discussion/Recommendation:

Phase 2 noted that new study will be submitted.

Guideline No.: 81-4 — Primary Eye Irritation/ Rabbit

MRID No.: None

Study No.: None — New study will be submitted for Phase 5.

Discussion/Recommendation:

Phase 2 noted that new study will be submitted.

Guideline No.: 81-5 — Primary Dermal Irritation/ Rabbit

MRID No.: None

Study No.: None — New study will be submitted for Phase 5.

Discussion/Recommendation:

Phase 2 noted that new study is required.

Guideline No.: 81-6 — Dermal Sensitization/Guinea Pig

MRID No.: None

Study No.: None — New study will be submitted for Phase 5.

Discussion/Recommendation:

Phase 2 noted that new study is needed.

Guideline No.: 81-7 — Acute Delayed Neurotoxicity/ Hen

MRID No.: None

Study No.: None — Not required.

Discussion/Recommendation: Not required.

Guideline No.: 82-1a — 90-Day Feeding/Rodent

MRID No.: None — New study will be submitted for Phase 5.

Study No.: None

Discussion/Recommendation:

Phase 2 noted that registrant will submit new study.

Guideline No.: 82-1b — 90-Day Feeding/Nonrodent

MRID No.: None — 90-Day dog study will not be needed since 1-year dog study will be required for Phase 5.

Study No.: None

Discussion/Recommendation:

Phase 2 noted that 90-day study is not needed.

Guideline No.: 82-2 — 21-Day Dermal/Rodent/Rabbit

MRID No.: None — New study will be required for Phase 5.

Study No.: None

Discussion/Recommendation:

Phase 2 noted that registrant will submit new study.

Guideline No.: 82-3 — 90-Day Dermal/Rodent

MRID No.: None — Not required.

Study No.: None

Discussion/Recommendation: Not required.

Guideline No.: 82-4 — 90-Day Inhalation/Rat

MRID No.: None — New study will be submitted for Phase 5.

Study No.: None

Discussion/Recommendation:

Phase 2 noted that registrant will submit new study.

Guideline No.: 82-5 — 90-Day Neurotoxicity

MRID No.: None — New study in mammals is required for Phase 5.

Study No.: None

Discussion/Recommendation:

Phase 2 noted that neurotoxicity symptoms were observed in several studies.

Guideline No.: 83-1a — Chronic Toxicity/Rodent

MRID No.: 415595-01 (7 volumes)

Study No.: IRDC No. 556-011

This study satisfies the requirement for Phase 5 for a chronic toxicity study in rodents (2-year rat study).

Discussion/Recommendation:

2-Year chronic toxicity/oncogenicity study (1990) in rats. Fulfills acceptance criteria. Has not been reviewed (9/21/90) but possible cancer problems in rats. However, NOEL for chronic toxicity is established at 100 or 1000 ppm.

Guideline No.: 83-1b — Chronic Toxicity/Nonrodent

MRID No.: None

Study No.: None

New study will be submitted for Phase 5.

Discussion/Recommendation:

Phase 2 noted that new study will be submitted.

Guideline No.: 83-2a — Oncogenicity/Rat

MRID No.: 415595-01 (7 volumes)

Study No.: IRDC No. 556-011

This study satisfies the Phase 5 requirement for a rat oncogenicity study. MTD is established at 3000 ppm based on decreased body weight gain. Possible cancer problems.

Discussion/Recommendation:

2-Year chronic toxicity/oncogenicity study (1990) in rats. Fulfills acceptance criteria for oncogenicity in rats. MTD based on 7 to 10 percent decrease in body weight gain in male and female rats. NOEL is 100 or 1000 ppm. Possible cancer problems. Thyroid tumors in females and skin tumors in males were increased at 3000 ppm.

Guideline No.: 83-2b — Oncogenicity/Mouse

MRID No.: 415594-01 (5 volumes)

Study No.: IRDC No. 556-013

This study satisfies the Phase 5 requirement for a mouse oncogenicity study.

Discussion/Recommendation:

This study filfills acceptance criteria. Study was completed in 1990. MTD based on effects at 5000 ppm (HDT) and results of range-finding study. NOEL appears to be 100 ppm.

Guideline No.: 83-3a — Teratology/Rat

MRID No.: 402882-01 and -02

Study No.: IRDC No. 566-002

Study is acceptable for Phase 5 review.

Discussion/Recommendation:

Phase 2 noted that this study is fully acceptable.

Guideline No.: 83-3b — Teratology/Rabbit

MRID No.: 402882-01 to -03

Study No.: IRDC No. 566-004

Study is acceptable for Phase 5 review.

Discussion/Recommendation:

Phase 2 noted that study is fully acceptable.

Guideline No.: 83-4 — Two-Generation Reproduction/ Rat

MRID No.: 413275-01

Study No.: IRDC No. 556-005

New study is acceptable for Phase 5 review.

Discussion/Recommendation:

New study not previously reviewed. Fulfills acceptance criteria without substantive changes.

Guideline No.: 84-2a — Mutagenicity/Ames

MRID No.: 413447-01

Study No.: T8729.501014

New Study is acceptable for Phase 5 review.

Discussion/Recommendation:

New study not previously reviewed. Fulfills acceptance criteria.

Guideline No.: 84-2b — Mutagenicity/Structural Chromosomal Aberration

MRID No.: 413446-01

Study No.: T8729.337

New study is acceptable for Phase 5 review.

Discussion/Recommendation:

New study not previously reviewed. Chromosome aberrations in CHO cells (in vitro) fulfills acceptance criteria.

Guideline No.: 84-4 — Other Genotoxic Effects

MRID No.: 413445-01

Study No.: T8729.38009

New study is acceptable for Phase 5 review.

Discussion/Recommendation:

UDS in rat primary hepatocytes. New study not previously reviewed. Fulfills acceptance criteria.

Guideline No.: 85-1 — Metabolism

MRID No.: None

Study No.: None

New study is required for Phase 5.

Discussion/Recommendation:

Phase 2 noted that new study is needed.

Guideline No.: 85-2 — Dermal Penetration

MRID No.: None

Study No.: None

Not required.

Discussion/Recommendation: Not required.

Guideline No.: 86-1 — Domestic Animal Safety

MRID No.: None

Study No.: None

Not required.

Discussion/Recommendation: Not required.

57378:I:Dykstra:Draft:LHED-9:KENCO:9/25/90:10/24/90:EK:JH:DD
R:57385:Dykstra:LHED-9:KENCO:10/10/90:11/09/90:ejh