US EPA ARCHIVE DOCUMENT

CASWELL

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

JAN 23 1997

012146

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

**MEMORANDUM**

SUBJECT: VINCLOZOLIN--Tox. Data Submitted Under MRID Nos. 41471005 and 92194019; TRID No. 470148-002

Tox Chem. No. 323C
Chemical: 113201
RD Record: [Not provided]
HED Project: D222318 F.S.
(DP Barcode):

FROM: Irving Mauer, Ph.D., Geneticist
Toxicology Branch-I
Health effects Division (7509C)
03-27-96

TO: Barry O'Keefe
Special Review and Reregistration Division (7508W)

THRU: Karen L. Hamernik, Ph.D., Head, Section III
Toxicology Branch-I
Health effects Division (7509C)
for Budd 1/7/97 KB

Registrant: BASF, RTP (NC)

Request: Review and evaluate the following mutagenicity assay (an Ames Test):

(84-2) Report on the Study of Vinclozolin (Reg. No. 83/258) (ZNT Test Substance 82/370) in the Ames Test, performed at BASF Laboratories in Ludwigshafen (West Germany), Reg. Doc. No. 83/0228, Final Report dated November, 1983. (MRID 41471005). UNPUBLISHED.

[NB: Two other documents were submitted with this study:

(1) "Report on the Study of Vinclozolin (Reg. No. 83-258) (ZNT Test Substance: 82/370) in the Ames Test", BASF Nov. 14, 1983. (TRID No. 470-148-002), which is an exact duplicate of the above study, and will not be separately reviewed.

Recycled/Recyclable • Printed with Vegetable Oil Based Inks on 100% Recycled Paper (40% Postconsumer)

(2) Phase 3 Summary of MRID 41471005 (the subject study), MRID 92194-019, which also will not be separately reviewed.]

TB CONCLUSION: This Ames Test (MRID 41471005) is ACCEPTABLE, in demonstrating Vinclozolin was negative for induced mutagenicity (reverse mutation) in Ames Testing, and thus satisfies data requirements for FIFRA Test Guideline 84-2a for this type of mutagenicity study.

(ATTACHMENT) DER



2

DISK 6:41471005:MAUER:MB

EPA Reviewer: Irving Mauer, Ph.D. _____, Date 05/29/96
Review Section 3, Toxicology Branch I (7509C)
EPA Secondary Reviewer: Karen L. Hamernik, Ph.D. _____, Date 1/7/97
Review Section 3, Toxicology Branch I (7509C) for Budd

# DATA EVALUATION RECORD

STUDY TYPE: Salmonella/Reverse Gene Mutation Assay (Ames Test) OPPTS 870.5265 [§84-2]

DP BARCODE: D222318 SUBMISSION CODE: [Not provided]
P.C. CODE: 113201 TOX. CHEM. NO.: 323C

TEST MATERIAL (PURITY): Vinclozolin (98.1% a.i.)

SYNONYMS: RONILAN

CITATION: H. P. Gelbke and G. Engelhardt (1983). Report on the study of Vinclozolin (Reg. No. 83/258) (ZNT Test Substance No. 82/370) in the Ames Test, performed at the BASF Aktiengesellschaft, Department of Toxicology, Ludwigschafen, West Germany. Doc. No. 83/0228, Final Report dated November 1983. MRID 41471005. Unpublished.

SPONSOR: BASF Corporation, RTP (NC).

EXECUTIVE SUMMARY: In a bacterial reverse gene mutation (Ames) assay (MRID 41471005), multiple cultures of *Salmonella typhimurium* TA strains (TA 1535, 1537, 1538, 98, 100) were exposed to test article in both the standard plate assay (all strains) and by pre-incubation (only TA 100) at concentrations up to 10,000 ug/plate.

No cytotoxicity was observed in any strain tested up to the HDT, and incomplete solubility was evident at 5000 ug/plate and above. No increased incidence of reverse mutation (revertant colonies) over DMSO (solvent) controls was found.

This assay is considered ACCEPTABLE in demonstrating no mutation in Salmonella TA strains, and satisfies data requirements for FIFRA Test Guideline 84-2a for this type of mutagenicity study.

COMPLIANCE: Signed and dated GLP, Quality Assurance, Data Confidentiality, and Flagging statements were provided.

# I. MATERIALS AND METHODS

## A. MATERIALS

1. Test Material: Vinclozolin

Description : White powder
Lot/Batch #: 82/370
Purity: 98.1% a.i.
Stability of compound: Said to be stable in solvent at 4°C.
CAS #: 50471-44-8
Structure: 3-(3.5-dichlorophenyl)-5-ethenyl-5-methyl-2.4-oxazolidinedione
Solvent used: Dimethylsulfoxide (DMSO)
Other comments: Test article precipitates out at 5000 ug/plate and above.

2. Control Materials:

Negative: None
Solvent/final concentration: 1%
Positive: Nonactivation:

4-Nitro-o-phenylenediamine, 10 ug/plate for TA 98 and TA 1538
9-Aminoacridine, 100 µg/plate for TA1537
Other: N-methyl-$N^1$-nitro-N-nitrosoguanidine (MNNG), 5 ug/plate for TA 100 and TA 1535.

Activation:
2-Aminoanthracene (2-anthramine), 10 µg/plate for all strains

3. Activation: S9 derived from

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| X | Aroclor 1254 | X | induced | X | rat | X | liver |
| ___ | phenobarbital | ___ | non-induced | ___ | mouse | ___ | lung |
| ___ | none | | | ___ | hamster | ___ | other |
| ___ | other | | | | | ___ | other |

Describe S9 mix composition (if purchased, give details):

MgCl2-8mM
KCl-33mM
Glucose-6-PO4-5mM
NADP-4mM
PO4-buffer-100mM
S9-3 volumes



5

4. Test organisms: S. typhimurium strains (all his⁻):

___ TA97 _X_ TA98 _X_ TA100 ___ TA102 ___ TA104
_X_ TA1535 _X_ TA1537 _X_ TA1538; list any others:
Properly maintained? Y
Checked for appropriate genetic markers: Y

5. Test compound concentrations used:

Nonactivated conditions: 100-10,000 ug/plate (4 plates per dose)
Activated conditions: 100-10,000 ug/plate (4 plates per dose)

B. TEST PERFORMANCE

1. Type of Salmonella assay:

_X_ standard plate test, all strains
_X_ pre-incubation (_8_ minutes), TA 100 only
___ "Prival" modification
___ spot test
___ other (describe)

2. Protocol: Procedure for the standard plate test was based upon the method of Ames (1973, 1975); that for the pre-incubation assay on Yahagi et al. (1977) and Matsushima et al. (1980).

C. REPORTED RESULTS:

1. Preliminary cytotoxicity assay:

There was no cytotoxicity in any strain up to the HDT, 10,000 ug/plate, with/without S9-activation. Incomplete solubility was observed at concentrations of 5,000 ug/plate and above.

2. Mutagenicity assay: In neither plate assay with all strains with/without activation, nor in the pre-incubation assay with TA 100 ± S9 activation, was there any increase in his+ revertant colonies over background (DMSO solvent control - Report Tables 1, 2 - attached here). In contrast, all positive control plates registered the appropriate increased revertents.

D. REVIEWER'S DISCUSSION/CONCLUSIONS: This assay was performed with conventionally recognized procedures to yield valid results. We agree with the investigators' conclusions that under the conditions this study, vinclozolin was not mutagenic in inducing reversions at the histidine locus of the Ames battery of TA strains.



6

E. Was test performed under GLPs (is a quality assurance statement present)? Y

F. Appendix attached? Y, Data Tables

Disk 6: 41471005.DER:MAUER:mb



8

Tox Rev. 012140

Page_____ is not included in this copy.

Pages 9 through 10 are not included.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product impurities.

_____ Description of the product manufacturing process.

_____ Description of quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

✓ FIFRA registration data.

_____ The document is a duplicate of page(s) _____.

_____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.