



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

DEC 1 1983

~~DEC 1 1983~~

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

TO: Robert Taylor, PM #25
Registration Division (TS-767)

THRU: Robert B. Jaeger, Section Head
Review Section #1
Toxicology Branch/HED (TS-769) *RTJ 11/22/83*
WHS 12/1/83

SUBJECT: Oryzalin 1471-96/1471-112: Registrant's Reply to the
Previous TB Review Comments Concerning the Rat Dominant
Lethal Study with Oryzalin Accession No. 248616;
CASWELL No. 623A.

Review of the Registrant's Responses to the Previous TB Review
Comments Concerning the Rat Dominant Lethal Study with Oryzalin
(TB Memo 1/20/83, J. Chen).

1. Insufficient Procedural Details and Treatment of Results:

a. The provided information of sequential mating in 7-day cycles for 10 successive weeks are considered to cover all stages of spermatogenesis in treated male rats. Although an expelled copulatory plug is a convenient means of timing a pregnancy, the vaginal swab technique should be also employed to detect the presence of sperm. The provided evidence of successive mating performance for the treated males during the entire mating period appears to be reasonable. The 2-day rest period between consecutive mating recommended for the male rats may not be critical in this case.

b. Generally, the parameters to score dominant lethality should be based on those that are sensitive to detect positive response and in discrimination against false results. We concur with the recently modified parameters for scoring dominant lethal effect by Green (1). The simplified parameters such as the implantation occurrence and resorption occurrence used in this study are considered adequate.

2. The Absence of Positive Control:

It is necessary to include a positive control with this report in order to ensure the proper responsiveness of the experimental animals. If Triethylenemelamine is used as the positive control, mating need not extend beyond 3 weeks.

3. The Absence of Vehicle Control:

The vehicle (negative) control used in this study is clarified.

4. Statements of Justification for the Selected Test Conditions in Performing the DML Test:

a. The supplemental information provided in the submitted Attachment II are acceptable. In addition, the use of five daily doses of 0.5 and 2 g/kg/day oryzalin to achieve the total doses of 2.5 and 10 g/kg respectively is considered adequate to meet the maximum dose requirements recommended for the dominant lethal test (2).

b. the supplemental explanation to support the 1:1 mating schedule provided in the submitted Attachment II is considered reasonable. According to the basic design of the study, 15 males and 150 females per dose group were used by the 1:1 mating schedule. The total numbers of female rats used in this study are considered comparable to the desired numbers of female rats provided by the customary 1:2 mating procedure (10 males and 160 females are customarily used).

5. Unclear Interpretation of Results:

The provided criteria for determining the positive response of oryzalin in this study are considered adequate.

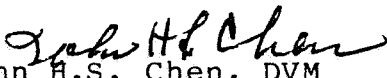
Recommendation:

With the exception of deficiency cited in our comments No. 2, the registrant's other responses to the previous TB review comments are considered adequate and acceptable.

References:

1. Green, S. (1980) "The Dominant Lethal and Heritable Translocation Test" Proceedings of A Workshop on Methodology for Assessing Reproductive Hazards in Work Place. National Institute of Occupational Safety and Health.

2. EPA Health Effect Test Guideline (1982): Rodent Dominant Lethal Assay, EPA 560/6-82-001.


John H.S. Chen, DVM
Review Section #1
Toxicology Branch/HED (TS-769)

TS-769:CHEN:s11:X73710:11/18/83 card 2