UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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JUN 20 1990

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Carcinogenic Dose Response Assessment of Oryzalin

TO: Jack Quest
Section Head
Science Analysis and Coordination Branch

FROM: Reto Engler, Chief
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Recently the HED Peer Review Committee considered the weight of the evidence concerning the carcinogenicity of Oryzalin, and in particular the appropriateness of using a low dose extrapolation model to quantify carcinogenic risks. At the original peer review meeting of September 16, 1985 Oryzalin was classified as a Group C carcinogen but no determination was made concerning the risk assessment mode for this chemical. However, in 1982 (prior to the publication of the EPA Cancer risk assessment guidelines) the data on Oryzalin was used to calculate and model a dose response for the purpose of a carcinogenic risk assessment (Memo of March 17, 1982 by B.D. Litt). At that time the basis for the dose response assessment were the skin tumors in both sexes of rats.

At the peer review committee meeting of June 13, 1990 the need for a dose response assessment was iterated by the committee, but it was concluded that the mammary tumors in female rats would be the more appropriate tumor upon which to base the low dose extrapolation model.

We have used the TOX-RISK Program of K.S. Crump to calculate the dose response slopes, i.e. the Q1* for Oryzalin. For the sake of comparing the 1982 calculation with the present program we also calculated the Q1* for the skin tumors as previously done by B. Litt. The correlation was very good, the Q1* calculated by Mr. Litt was 3.375 E-2 the one obtained by the TOX-RISK program was 3.2E-2.

As recommended by the peer review committee we calculated the Q1* based on the female mammary gland tumors. In the first attempt

we included all dose levels, however, the model fit was not very good since the tumor response at 900 and 2700 ppm was about the same. The Q1* based on the tumors at all the doses is 4.4E-2. However, since the top dose also was also considered to cause excessive toxicity (accelerated deaths toward the end of the study) and the data of the control, low-, and mid-dose show a very good fit to the dose response model it was concluded that the elimination of the top dose for the purpose of the dose response assessment was biologically justified. Using the low, and mid dose tumor response only the appropriate Q1* for Oryzalin was calculated to be 1.3 E-1 (mg/kg/day)E-1.

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