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

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MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Oryzalin Registration Standard - Oncogenic Studies on Oryzalin in Rodents [623A]

TO: Robert Taylor/James Yowell
Product Managers (25)
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Registration Division (TS-767)

THRU: Robert B. Jaeger
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Toxicology Branch is asked to comment on the oncogenic potential of oryzalin to humans from the final evaluation of long term oncogenic studies in mice and rats.

Following our previous review of the 2-year feeding/oncogenic study in the rat (TB Memo 1/7/81 M.L. Quaife), the 2-year feeding/oncogenic study in the mouse (TB Memo 10/7/81 M.L. Quaife), and the carcinogenicity/oncogenicity assessment of the 2-year feeding/oncogenic study in the rat (TB Memo 3/17/82 B.D. Litt), we have reached the following conclusions:

1. In the 2-year mouse oncogenic study, oryzalin was negative for oncogenicity in the mouse at up to 3650 ppm in the diet (highest level fed).

2. In the 2-year rat oncogenic study, large numbers of tumor bearing animals were identified in both control and treated animals. Statistical evaluation of the 2-year rat chronic feeding/oncogenicity study indicated that the incidence of thyroid tumors (follicular cell adenoma and C-cell adenoma) was not considered a significant finding. However, the skin tumors (keratoacanthoma and/or squamous cell carcinoma and basal cell and related tumors) were significantly increased in the treated group as compared to the control group. Therefore, TB considers oryzalin to be a rat oncogen.

1 of 2

PC 104201

3. According to the Guidance for Analysis and Evaluation of Long Term Rodent Studies Recommended by EPA-OPTS (Paynter 12/1/84), the most persuasive evidence of potential oncogenicity in man should come from competently designed and conducted human epidemiology studies supported by appropriate animal studies. Since no human epidemiology study for oryzalin is available to the Toxicology Branch, and since the results of oncogenicity experiments provide positive response in only one specie with no decrease time to tumor incidence, the availabe data provide only limited evidence that oryzalin is oncogenic to experimental animals. The weight of evidence from these long term rodent studies may be classified in the category of Group C- Possible Human Carcinogen (See also the Guidance recommended by Paynter). Tox Branch has been regulating oryzalin on the basis of this rat oncogenicity study and the subsequent risk assessment (Litt, 3/12/82) since 1982 and therefore, special review of these studies appears unnecessary at the present time.

Reference:

Paynter, O.E. Evaluation Procedures for Oncogenic Potential: Guidance for Analysis and Evaluation of Long Term Rodent Studies, EPA - OPTS, Revised December 1, 1984

2