1-8-85

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

004200

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Recommendation for Revision of Metolachlor Risk Assessment, Acc. No. 255592, Caswell #188DD

TO: Richard Mountfort PM#23
Registration Division (TS-767C)

FROM: Gary J. Burin, Toxicologist
Section V, Toxicology Branch/HED (TS-769)

THRU: Laurence D. Chitlik, DABT
Section Head, Section V
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THRU: Theodore Farber, Chief
Toxicology Branch/HED (TS-769)

Recommendations/ Discussion:

It is recommended that the metolachlor risk assessment be revised to take into account the most recent chronic rat study. The previous risk assessment (using the earlier rat study, the multistage model and GLOBAL program) generated a Q_1^* of 2×10^{-3} for this compound. Because the second study was intended to supercede the "Supplementary" IBT study, it is recommended that a new risk assessment be conducted. Deficiencies in the IBT study were noted in the memos of August 14, 1979 and December 17, 1979 from Larry Anderson and the memo of July 28, 1981 from this reviewer and Laurence Chitlik. The deficiencies included inadequate clinical chemistry determinations and diet preparation records.

It is noted that the determination of the oncogenic potency of this compound has assumed added significance in light of the fact that metolachlor is the primary alternative for alachlor (for which the Agency has recently issued a PD 1 expressing concern for potential oncogenicity risks).

It is also recommended that the second chronic rat study be be upgraded to "Core Minimum" status. This study was reviewed in my memo of December 14, 1983 and was classified as "Supplementary Data" pending resolution of the issue of apparently conflicting

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incidences of liver tumor reported in the study. This issue has now been satisfactorily resolved. A laboratory audit of this study was recently conducted and it revealed no deficiencies which would preclude this study from being classified as "Core Minimum" (see my review of September 20, 1984). The rereading of the liver slides continues to support the finding of an increased incidence of proliferative hepatic lesions in the high dose group (not significant in males, $p<0.01$ for females). See attached table taken from the recent submission.

cc: Reto Engler

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TABLE 4

Liver Histopathology Data from the EPL Reading of the Hazleton-Madison Study

Lesion[1]	Dose (ppm)							
	Male				Females			
	0	30	300	3000	0	30	300	3000
Number of Animals	60	60	60	60	60	60	60	60
Neoplastic Nodules	1	1	0	4	0	1	2	6*
Hepatocellular carcinoma	2	1	3	3	0	0	0	1
Total Number of Animals with Proliferative Lesions	3	2	3	7	0	1	2	7**

[1]An overall Chi-square analysis was conducted for each lesion by sex. If the Chi-square analysis showed significance at $P<0.05$, then a Fisher's exact test was performed to delineate differences from the control. Significant differences in Fisher's exact test are indicated by: *=$P<0.05$; **=$P<0.01$.

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