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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

DATE: July 28, 1981

SUBJECT: Draft Summary of January 27, 1981 Metolachlor Meeting with Ciba-Geigy

FROM: Gary J. Burin, Toxicologist
Toxicology Branch/HED (TS-769)
and
Laurence D. Chitlik, Section Head
Toxicology Branch/HED (TS-769)

LDC 7/28/81

TO: Jim Stone (23)
Registration Division (TS-767)

THRU: William Burnam, Acting Chief
Toxicology Branch/HED (TS-769)

WSB

The following comments pertain to the draft summary of the meeting held on January 27, 1981 between G. Burin, L. Chitlik, Jim Stone, EPA, and Gene Holt, Jack Norton and Darrel Sumner of Ciba-Geigy.

1. p. 1, first sentence, Metolachlor is misspelled.

2. p. 1, third paragraph, second sentence. This sentence is misleading. An "argument" was not made by Ciba-Geigy regarding the importance of this study and its' necessity in the establishment of tolerances for potatoes, cottonseed and seed and pod vegetables; the fact that a valid classification of this study would result in a lower TMRC was simply mentioned in passing. Tolerances are not directly tied to this study.

3. p. 1, third paragraph, third sentence. The statement that "1000 ppm is effect level" is not a direct quote from the Ciba-Geigy sponsored audit by Drill, Friess, Hays, Loomis and Shaffer, Inc., as is implied in your summary. What the audit report actually stated was:

   "It seems that a case could be made for a significant effect at the 1000 ppm level (T-III). However, in the absence of appropriate analysis (and the presence of numerous inappropriate ones) it is difficult to reach a firm conclusion."

   Furthermore, it should be noted that the above quote refers only to body weights and not to the study as a whole.

4. p. 1, third paragraph, final sentence. The word "supplemented" should be changed to read "Supplementary Data."

5. p. 2, final sentence. The "bottom line" of the meeting is not accurately presented. Our branch policy requires that a chronic feeding study establish a NOEL - this study does not do so. The Ciba-Geigy consultants do not claim that a NOEL for this study was established.

   An important omission from the draft memo is mention of the failure of IBT to follow their stated procedure, specifically to follow up any effects on hematology and clinical chemistry at lower dose levels. This was the primary issue of the meeting.

   Although not available at the time of the meeting, a recent submission, the 6 month interim report from a two year chronic rat study now underway for Metolachlor (Acc. No. 244166) appears to give further support to the hypothesis that the effect on Serum Glutamic Oxalacetic Acid observed in 3000 ppm males was biologically as well as statistically significant and thus should have been followed up at lower levels to determine the level at which an effect on SGOT would not be observed i.e. the NOEL. Although we agree that the IBT study contains useful information, the lack of a NOEL for SGOT (and possibly other parameters) combined with the deficiencies outlined in the memos of August 14, 1979 and December 17, 1979 from L. Anderson prevent this study from attaining "Valid" status. However, based on the available raw data and our analysis of the conduct of the study we recommend that it be considered "Supplementary" as both an oncogenicity and a chronic feeding study.

cc: Jan Auerbach, SPRD

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WASHINGTON, D.C. 20460

Draft

MEMORANDUM

SUBJECT: Meeting held to discuss 90 day and 2 year rat feeding studies conducted with metolachlon.

TO: Files - Metolachlor Standard
"Dual 8E" EPA Reg. Number 100-597
"Metolachlon Technical" EPA Reg. Number 100-587

Participants:

Ciba-Geigy Corp	EPA
Gene Holt, Ph.D.	Gary Burin, Tox Branch, HED
Jack Norton, Ph.D.	Larry Chitlik, Tox Branch, HED
Darrel Sumner, Ph.D.	Jim Stone, PM-23, RD

On January 27, 1981 a meeting was held to discuss the above two toxicology studies submitted to support registration of metolachlor

The metolachlor standard stated that a complete histopathology review of the 90 day rat feeding must be submitted. At the meeting it was agreed that a histopathology review of the 1 year interim sacrificed rats in the two year chronic feeding study currently underway would supersede the requirement for the 90 day study. Ciba-Geigy will write a letter agreeing to submit the review of the interim sacrificial rats.

The standard stated that the IBT 2 year study was invalid for chronic effects. Ciba-Geigy presented their argument that the IBT 2 year rat study was very important to their company since if the Agency decided it was Core Minimum Data this would allow the percentage of the Maximum Permissible Intake to be lowered from 60% to approximately .15% and thus additional tolerances could be established including potatoes, cottonseed, and seed and pod vegetables. The highlights of the retrospective audit of the 2 year study conducted by Drill, Friess, Hays, Loomis & Shaffer, Inc. were presented including the statement "It is concluded that the complete set of data is of sufficient quality to afford a basis for regulatory decision-making" and "1000 ppm is the effect level." Larry Chitlik and Gary Burin had reviewed the retrospective audit. They concluded that the study is supplemented for determining chronic effects in rats - containing valuable

information - but not Core-Minimum Data since a NOEL level could not be determined. Hematology, clinical chemistry and urinalysis were presented only for the control and high dose. There were statistically significant differences between the control and high dose in this study. The bottom line is that the Ciba-Geigy and the consultants state that there is enough information to use this study to establish further tolerances, but Toxicology Branch, based on this study, cannot determine the No Observable Effect Level for chronic effects to rats.