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HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

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MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: **SAN 835 H AI:** Mouse Carcinogenicity Study Protocol - Study Termination Time; Two-Generation Reproduction Study Protocol

TO: Karen Hicks
PM Team Reviewer (25)
Registration Branch, RD (7508C)

FROM: Linda L. Taylor, Ph.D. Linda Lee Taylor 2/23/95
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Health Effects Division (7509C)

THRU: K. Clark Swentzel K. Clark Swentzel 2/23/95
Section II Head, Toxicology Branch II
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and

Marcia van Gemert, Ph.D. marcia van gemert 2/24/95
Chief, Toxicology Branch II/HFAS/HED (7509C)

Registrant: Sandoz Agro Ltd.
Chemical: SAN 835H
Synonym: none provided
Submission No.: S478981
DP Barcode: D210489
Caswell No.: ?
Case: 286172
Shaughnessey No.: 114501
MRID No.: N/A
Action Requested: Please review the attached.

Comment: The Registrant has submitted two study protocols that conform to OECD guidelines [Mouse Carcinogenicity Study and Two-Generation Reproduction Study]. At issue is the study termination time for the mouse carcinogenicity study.

The protocol for the Mouse Carcinogenicity Study [Study # 549M] states that the main group of mice will be terminated when one of the following criteria has been met: (1) if at the end of week 78 mortality of the controls [both sexes combined] is in excess of 30%, the entire study will then be terminated; (2) if the study proceeds beyond 78 weeks, each sex will be terminated separately when survival in the group of highest mortality for that sex approaches 50% mortality; (3) the study will be terminated

regardless of mortality status at 104 weeks. These criteria are adequate and essentially encompass those of the FIFRA guidelines.

The protocol for the two-generation reproduction study is adequate and a study would be accepted if conducted as per protocol. However, there are several aspects that are not included, which, following a review of the data from the study, may be necessary to adequately evaluate the effects. The following aspects have not been provided for: (1) an assessment of estrous cycle length and normality prior to mating; (2) sperm analyses of all P and F1 males; (3) an assessment of developmental milestones; (4) brain, kidney, adrenals, spleen, and thymus weights for all P and F1 parental rats and all F1 pups examined macroscopically; (5) quantification of oocytes; and (6) no histopathology of the weanlings is mentioned.

CONCLUSION

The submitted protocols, which conform to OECD guidelines, are both acceptable to the Agency. The specific issue addressed in the cover letter dated 12/13/94 was the study termination time for the mouse carcinogenicity study. The criteria to be utilized in determining when the study will be terminated are adequate and acceptable to the Agency. There was no specific protocol issue highlighted for the two-generation reproduction protocol. Depending on the outcome of that study, the assessments noted above as not being addressed by the protocol may be necessary to fully assess any reproduction and fertility effects of SAN 835H.