272E

CASWELL FILE

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

JUL - 9 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Cyproconazole: Pathology Report Summary of 13-Week Feeding Study in Rats - Marked 6(a)(2)

TO: Denise Greenway
PM Team Reviewer (21)
Registration Division (H7509C)

FROM: Linda L. Taylor, Ph.D. Linda Lee Taylor 7/1/93
Toxicology Branch II, Section II
Health Effects Division (H7509C)

THRU: K. Clark Swentzel K. Clark Swentzel 7/6/93
Section Head II, Toxicology Branch II
Health Effects Division (H7509C)

and

Marcia van Gemert, Ph.D. Marcia Gemert 7/7/93
Chief, Toxicology Branch II, HED (H7509C)

Registrant: Sandoz Crop Protection Corporation
Chemical: α-(chlorophenyl)-α-(1-cyclopropylethyl)-1H-1,2,4-triazole-1-ethanol
Synonyms: Cyproconazole Technical
Caswell No.: 272E
Case : 193784
Submission: S440311
Barcode: D191014
Identifying No.: 055947-RGG
Shaughnessy No.: 128993
MRID No.: 427449-00 & 01
Action Requested: Report submitted as 6(a)(2), however, SWAT team determined that the cited action is not a priority. Please review and add to your files on the chemical Cyproconazole.

Comment: The Registrant has submitted a "draft" introduction and summary page of the pathology report of a new 13-week Wistar rat feeding study [TB II notes that the page is not marked draft].

The report states that (1) there is an increase in the incidence and severity of hepatocellular centrilobular hypertrophy and vacuolation in the livers of males and females at dose levels of 350, 700, and 1400 ppm; (2) at 700 and 1400 ppm, the number of macrophages in the spleen and blood vessels of the lungs, liver, (1)

and kidney is increased; (3) an increased level of brown pigment deposits in the renal tubular epithelium was observed in females at 1400 ppm; and (4) the incidence and severity of thyroid microfollicular epithelial hypertrophy, which was considered to be an adaptive response rather than a toxic change by the author, was increased at 350, 700, and 1400 ppm in both sexes. Based on the liver effects, the "dietary no toxic effect level (NTEL)" was determined to be 20 ppm.

The liver effects are similar to those observed in the mouse study and are not unexpected. An effect on the thyroid has not been reported previously. Additional data/information are necessary before a determination of whether the noted effect is an adaptive response or an antithyroid effect.

TB II will review the 13-week study when it becomes available. No further action is necessary at this time.