Caswell File
6-12-87
006504

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

JUN 12 1987

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Propazine: Quantitative Risk Assessment of Two-Year Chronic Oral Study in Female Rats (IRDC Report No.382-007; April 28, 1980). Caswell # 184.

FROM: C.J. Nelson, Statistician
Scientific Mission Support Staff
Toxicology Branch, HED (TS-769)
cjnelson 6/12/87

TO: William Dykstra, Ph.D., Toxicologist
Section III
Toxicology Branch, HED (TS-769)

THRU: Richard Levy, M.P.H.,Leader-Biostatistics Team
Scientific Mission Support Staff
Toxicology Branch, HED (TS-769)
Richard Levy 6-12-87

and

Reto Engler, Ph.D., Chief
Scientific Mission Support Staff
Toxicology Branch, HED (TS-769)

Summary:

The potency estimate, Q_1^*, of Propazine [C(q)] is 1.7×10^{-1} $(mg/kg/day)^{-1}$ in human equivalents. This estimate was calculated using the Weibull '82 model and is based upon All+ mammary tumors combined in female rats.

+ Mammary Gland: Adenoma and/or Adenocarcinoma, Papillary Adenoma and/or Adenomacarcinoma, Fibroadenoma, Cystadenoma, Ductular Adenoma.

Quantitative Risk Assessment:

Since there were significant survival disparities between control and dose groups in the two-year chronic oral study of female rats fed propazine, the potency estimate, Q_1^*, was obtained using the Weibull '82 time-to-tumor model for extra risk. (Reference memo on Qualitative Risk Assessment of Propazine - R. Levy 4/87). The resulting potency estimate in $(ppm)^{-1}$ of Propazine was converted to $(mg/kg/day)^{-1}$ for rats by using Lehmannn's Tables and then to human equivalents in $(mg/kg/day)^{-1}$ on the basis of an interspecies surface area adjustment as recommended by the EPA Cancer Guidelines.

The potency estimate based on all mammary tumors combined in female rats fed propazine for 105 weeks was 1.7×10^{-1} $(mg/kg/day)^{-1}$ human equivalents. A potency estimate was also calculated for malignant tumors combined and was 5.9×10^{-2} $(mg/kg/day)^{-1}$ human equivalents. For comparison, the human equivalent potency estimate on all mammary tumors combined was 1.3×10^{-1} $(mg/kg/day)^{-1}$ and the human equivalent potency estimate on malignant mammary tumors combined was 5.3×10^{-2} $(mg/kg/day)^{-1}$ using the Crump multistage procedure.