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8ENq-0681-03943 Follow-up
88-8100346

TITLE: Protocol for Oral Teratology Study of T2000C0[A] in Rats

OBJECTIVE: A teratology study will be used to evaluate the embryotoxic and teratogenic effects of orally administered T2000C0 to pregnant rats during the period of organogenesis. The procedure complies with the general recommendations of the FDA issued in January, 1966 ("Guidelines for Reproduction Studies for Safety Evaluation of Drugs for Human Use"). The study will be conducted according to the 1978 Good Laboratory Practice Regulations and

SPONSOR:

TESTING FACILITY:

STUDY DIRECTOR:

START OF DOSING: April, 1981.

TEST SYSTEM: One hundred and ten sexually mature, time mated Sprague-Dawley derived female rats from Charles River Breeding Laboratory will be housed in hanging stainless steel cages with wire mesh floors and fronts in a temperature and humidity controlled room. This strain of rat will be used because of historical control data and time mated females are readily available. Purina Laboratory Chow and water will be available ad libitum. The lights will be on a 12 hour light/dark cycle.

TEST SYSTEM IDENTIFICATION: Each animal will be ear tagged and that number will be indicated on the outside of the cage.

RANDOMIZATION: The animals will be assigned cages according to a computer-generated random numbers table.

CONTROL ARTICLE: Corn oil.

TEST ARTICLE: T2000C0.

ANALYTICAL SPECIFICATIONS: The test article, composition and purity will be determined by the Sponsor prior to the start of the study and at the end of dosing.

DOSAGE LEVELS AND ADMINISTRATION: The test article will be suspended in corn oil daily. The test article suspension and control article will be administered by oral intubation to the rats on days 6 through 15 of gestation according to the following:

[A] PC-143

Dose Level	Group Size
150 mg/kg/day	22
5 mg/kg/day	22
1.5 mg/kg/day	22
0.05 mg/kg/day	22
0 mg/kg/day	22

The oral route of administration will be used because metabolism studies showed radiolabeled Tepraloxydim was well absorbed. No dietary contaminants are known to interfere with the test article.

The animals will be observed daily from day 3 through day 20 of gestation for abnormal clinical signs. Body weights will be recorded on days 3, 6, 9, 12, 15 and 20 of pregnancy and the dose dosed accordingly using a constant dose volume of 5 ml/kg of body weight.

The females will be killed on day 20 and the ovaries, uterus and its contents will be examined to determine: number of corpora lutea, number of fetuses (live and dead), number of resorption sites, number of implantation sites, pup weight and gross abnormalities. Approximately one-third of the pups will be fixed in Bouin's solution for subsequent free-hand sectioning by the Wilson technique to determine any visceral abnormalities using a dissecting microscope. Select five sections can be sent to histopath of microscopic examination as deemed necessary by the study director. The remaining approximately two-thirds of the pups will be fixed in ethyl alcohol for subsequent skeletal examination after clearing and staining with alizarin red.

DATA ANALYSIS AND FINAL REPORT: The proposed statistical methods to be used for analysis of the data are: Dunnett's t test for dam and pup weights, number of fetuses, number of resorption sites, number of implantation sites and number of corpora lutea; Chi square for percent abnormalities. The proposed date for the final report is 2-3 months after detailed pup examinations have been completed (approximately third quarter, 1981).

The following was a hand written note to the study file.

The control article for (Oral Teratology Study of T-2998CoC in Rats) will be changed from corn oil to water. The test article will not be suspended in corn oil daily as noted in the protocol, but solution will be made by dissolving T-2998CoC in water by and the solution for the whole study will be submitted to 3M Commercial Chemical group for clearance before the start of the study and at the end of dosing.

4-3-81