

MATERIAL FROM FOOD AND DRUG ADMINISTRATION
FILES ON BIPHETAMINE AND IONAMIN

SUMMARY OF NDA 11-613

STRASENBURGH LABS, ROCHESTER, N.Y.,
Original Appearance Date: December 2, 1957.

Name of drug: Trade—Ionamin "15", Ionamin "30". Generic—Phentermine resin (Phentermine complex on cation exchange resin).

Dosage: Oral—1 capsule, sustained release, 15 or 30 mg/day.

Category: Anorexic.

Material reviewed:

Study 1.—Six months "chronic" administration in Rat and Dog. International Research and Development Corp. June 22, 1964.

Study 2.—Three litter breeding cycle in Rat. International Research and Development Corp. Part 1—2 litter. October 19, 1963, 3rd litter February 14, 1964.

Study 3.—"Newborn mortality study". Strassenburgh Lab. March 25, 1965 (actually a 1-cycle reproduction study).

PHARMACOLOGIST'S SUMMARY

Study 1.—Rats were given 10, 25, and 50 mg/kg/day phentermine HG1 by gavage seven days a week for 26 weeks. There were 20 males, 20 females in control and high dosage groups and 15 males, 15 females in another two. There was less weight gain on drug which was most evident in males and was dose related. Food consumption was slightly higher on drug. No significant differences in survival, nor were there drug related deaths or pathology. The most frequently observed drug related symptom was hyperactivity which was marked at 50 mg/kg. Occasional alopecia occurred at this level (83 x HO).

Beagle dogs (2 male, 2 females at each level) were given 5, 10, 15 mg/kg/day RC1 phentermine in 2 divided doses, for 26 weeks). An additional 4 dogs received 1 or 2 doses each of 20 or 40 mg/kg Mydriases, tachycardia, and hyperactivity were the principal drug and dose related signs. Lethargy prior to 1st half of daily dose was seen at 10 and 15 mg/kg. *One animal at each of these levels died during test periods. After one dose of 20 mg/kg 3 dogs died within 4½-7 hours and the other in less than 24 hours. Three dogs died after one 40 mg/kg dose in 4-8 hours and the other 1 hour after second dose. Weight gain was normal at 5 mg/kg but weight losses occurred at higher doses. Appetite decreased during initial weeks but returned to normal after 5th week. No apparent drug induced hematologic or pathologic changes were seen.*

Study 2.—This reproduction rat study included 20 males and 20 females given 40 mg/kg/day (70 x HTD) Phentermine resin by gavage thru three breeding cycles. During the third cycle drug administration was stopped 10 days after pairing. The reproductive performances are shown in the following table:

Cycle and drug	Percent pregnancy	Live fetuses per litter	Dead fetuses per litter	Birth weight	21 day survival per litter	21 day weights M
1. Control.....	80	10.0	0.38	6.4	9.8	39.4 3
Ionamin (40).....	79	7.3	1.00	5.5	3.1	20.5 1
2. Control.....	79	9.5	0.87	5.9	8.9	38.1 3
Ionamin (40).....	67	8.8	0.80	5.5	2.4	27.2 2
3. Control.....	93	8.1	0.92	6.3	8.1	43.7 4
Ionamin (40).....	80	7.8	1.25	6.1	7.1	42.6 4

(15267)