MEMORANDUM

FOOD AND DRUG ADMINISTRATION,
February 17, 1959.

To: New Drug Branch.
Attention: Dr. DeFelice.
From: Division of Pharmacology.
Subject: Ionamine Resin (R. J. Strasenburgh Co.)

On the basis of the animal toxicity work in rats and dogs, the compound appears to be safe at a dosage of 30 mg per day. There were a large number of deaths in the rats which were attributed to tubing errors. No evidence of drug toxicity was observed either grossly or historically.

In my opinion, the clinical studies appear pretty weak especially with regard of the duration of drug administration, but that decision is up to you.

E. I. GOLDENTHAL.

MEMORANDUM

FOOD AND DRUG ADMINISTRATION,
January 16, 1964.

To: Division of New Drugs.
Attention: Dr. A. G. Pleron.
From: Dr. William D'Aguanna, Division of Pharmacology.
Subject: Ionamine Resin (Phentermine Resin Complex), R. J. Strasenburgh Co., Rochester, N.Y. AP 13–460.

The culmination of 10–28–63 contains a subacute oral rat study and a 2 litter rat reproduction study.

I. Subcute Oral Rat Study: In order to find a sub-toxic dose for a subsequent reproduction study, Ionamine Resin Complex was administered once daily for 5 wks to 4 groups of 10 rats each at 20, 40, 80 and 100 mg/kg.

Results: Drug was well tolerated at 20 and 40 levels but hyperactivity and diminished growth rate occurred at all levels. Alopetia appeared at the 40 level but mortalities (1/10 and 7/10) occurred only at 80 and 100. Except for fact of necrosis in the livers of 1 rat at the 20 and 2 at 120 levels, pathology was not remarkable, 40 mg/kg was chosen to be the subtoxic dose.

II. Two litter Reproduction Study: Ionamine Resine Complex was administered at 40 mg/kg to rats in a reproduction study essentially similar to one we are recommending.

Results: There was no evidence of teratogenicity and incidence of pregnancy, fetal development and av. litter size were normal. But the following adverse effects occurred:

(1) Parental mortality was increased in treated group (10/40 for treated vs 1/40 for control). Other than 1 death at 7th week, all the other deaths occurred between the ??th and 27th weeks of administration. This could seem to reflect a cumulative toxic effect which was not observed at this dose level in the 6 wk. subacute study.

(2) Parental body weights of treated were below controls. In the case of males, the av. weight was 40% below control whereas females weighed only 10% less.

(3) While the av. weight of newborns was only slightly less, two litters showed marked growth repression. This pattern of growth retardation was much more striking * * *

MEMORANDUM

FOOD AND DRUG ADMINISTRATION,
October 29, 1965.

To: Division of New Drugs/IND Branch
Attention: Dr. F. O. Kelsey
From: Dr. S. Hsia. DTE/Drug Review Branch.
Subject: IND 1133, (NDA 11–613) Progress Report, 4/8/65.
Name of Sponsor: Strasenburgh Laboratories, Rochester, N.Y., AF 13–460.
A. Organization Performing Toxicity Studies (Project Rapid)
(1) Reference Sponsor Above