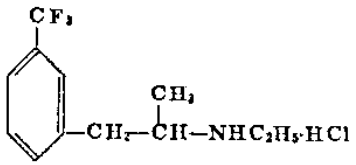
2. *Robert O. Knox, M.D., recommended a not-approvable letter on* May 19, 1969. Application was considered withdrawn on July 18, 1969, and reassigned for review with respect to safety and efficacy.

I. Category: Appetite Suppressant

II. Structural formula:



III. Dosage recommended: 20 to 40 mgs. TID.

IV. Related drugs: The amphetamines.

V. Pharmacology: Review dated February 19. 1969, states the drug appears to present no problem of safety and that the present labeling is acceptable.

VI. Consultation with other divisions: None.

VII. Clinical studies:

A. *Investigators.*—Five investigators performed special studies. Eight investigators performed controlled clinical studies. Ten investigators performed non-controlled clinical studies. Two investigators performed "other" clinical studies. The investigators' curriculum vitae appears adequate and they are considered acceptable.

B. *Clinical conditions.*—Patients are all said to be overweight; many had associated diabetes and hypertension.

Evaluation of the studies.—Study No. 2002, Investigator John A. Owen, M.D., Charlottesville, Virginia.

Study Design: Compared Ponderex with Methamyhetamine and a placebo in order to determine anorexic properties and side-effects of Ponderex alone, methamphetamine alone, and the combination. It was double-blind and crossed-over, two weeks on each of the four treatments with no diet prescribed. Patients used were ten female and two male, of which ten were diabetic, one an arthritic, and one normal individual. Of the ten diabetics, three were on no medication, one was taking Orinase, one was taking Hydroton, two were taking Dymalor, and two were taking Insulin. All patients took all four treatments.

Dosage schedule.—(1) Fenfluramine, 40 mg/day; (2) Methamphetamine, 2.5 mg/day; (3) Placebo; and (4) a combination of Fenfluramine 40 mgs and Methamphetamine, 2.5 mgs, given once daily. All treatment periods were 14 days.

Results showed a slight weight gain with the Fenfluramine and a slight weight loss with the Placebo.

Conclusion.—Data does not support efficacy for Ponderex with regard to its anorexic claim. It does support a claim of being less stimulating to C.V. system than the amphetamine (slight decrease in blood pressure and pulse rate with test drug compared with Ponderex).

Study No. 2009, Investigator Solomon Fisch, M.D., V. A. Hospital, Bronx, New York.

Study design.—Comparison of the safety and efficacy of Fenfluramine, Dextroamphetamine and a placebo. Low calorie diet was not prescribed.

The patients were divided into four groups and the results were as follows:

1. Dextroamphetamine group; fifteen subjects; five completed the study. There was a weight gain in two of the subjects and a weight loss in three of 5–10 lbs.

2. Placebo group; fifteen subjects; nine completed the study. There was a weight loss in six of 5–10 lbs. and a weight gain in three.

3. Fenfluramine group (20 mg TID); fifteen subjects; seven completed the study. There was a weight loss in all seven subjects, five lost less than 10 lbs. and three lost more than 10 lbs.

4. Fenfluramine (40 mgs TID) group; fifteen subjects; eight completed the study. There was a weight loss in five (three lost less than 10 and two lost more than 10 lbs.).

Comment and evaluation.—Subjects completing the studies were not enough to make a significant evaluation therefore data is not substantial. It is also noted that the heights are not given for any of the subjects in the study. An accurate diagnosis of overweight should have the height and weight determined for each individual. The results of this study does not adequately support anorexic claim