MEDICAL OFFICER'S REVIEW OF NDA 16-618

ADDENDUM NO. 2

MAY 6, 1969.

Sponsor.—A. H. Robins Company Inc., 1407 Cummings Drive Richmond, Va. 23220. Chemist: C. Lockett, Pharmacologist: V. Clocklin, Ph. D.

Product.—Ponderex.

Original review.—August 29, 1967 by Dr. R. Zoppa (Vol. 1.1) which contains no conclusions as such, but on page 17 under Labeling Evaluation states: "The labeling for Ponderex (*fenfluramine* hydorchloride) in my opinion gives full disclosure. The sponsor's claim that the drug is an appetite-suppressant indicated as adjunctive therapy in the medical management of exogenous obesity would appear to be supported by the studies submitted. The statements made in the labeling that fenfluramine's primary CNS effect appeared to be sedative and that it has little propensity for producing pressor effects compared to D-Amphetamine seem to be substantiated by the studies."

On February 2, 1968 an additional note was made by Dr. Zoppa (Vol. 21): "The revised labeling (package insert) submitted on 12/15/67 has all the labeling changes agreed upon in the 9/20/67 conference between sponsor and OND."

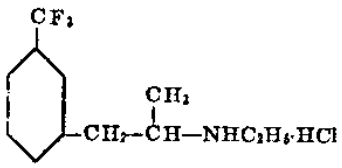
On June 20, 1968 the FDA sent an "inadequate" letter containing the statement that four of the control clinical studies with Ponderex subjected to statistical analysis revealed deficiencies in the study design that placed in question the efficacy of Ponderex as an anorexigenic agent."

On November 5, 1968 we received amendments consisting of 14 additional volumes of study summaries, raw data and other information, including a revised package insert.

Due date: May 5, 1969.

I. *Category.*—Appetite suppressant.

II. *Structure formula.*—



III. *Dosages recommended.*—20 to 40 mg t.i.d.

IV. *Related drugs.*—The amphetamines.

V. *Pharmacology.*—Pharmacologist's review dated February 19, 1969 states that the preclinical information in this resubmitted NDA for Ponderex does not change our previous evaluation of August 20, 1967 and January 29, 1968 that the drug appears to present no problem of safety and that the labeling is acceptable.

VI. *Consulations 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.

In general, the physicians listed appear technically qualified; however, I have reservations about the validity of work done by Dr. Daneman because of the work submitted by him in connection with a thiazide diuertic several years ago.

B. *Clinical conditions*

The diagnosis of obesity is frequently not backed up with data as to the height of the patients; therefore, it is impossible to make a determination as to the degree of obesity present.