MEMORANDUM OF CONFERENCE

A. H. ROBINS CO., INC.,
Richmond, Va., September 11, 1968.

Present: R. Dent, Jr., M.D., E. Woodward, Jr., M.D.—A. H. Robins Company, Inc., R. Murphey, Ph. D., Mr. L. Preston, Jr., and M. L. Gibson, M.D., Director, DND/OND/Med/FDA, Robert O. Knox, M.D., Mr. Peter James—SA/DS/Med/FDA.

The visitors came not to discuss the protocol but to dispute our decision that the data submitted to date was inadequate to demonstrate safety and efficacy. Therefore, Mr. James went through his memo of August 9, 1968 addressed to Acting Director, DND. Our visitors disputed many of the points, including, for example, the statement that in Finnerty's study the drug group averaged 233 pounds initial weight vs. 171 pounds for the placebo subjects and that this would introduce a bias.

We were advised that approximately seven or eight hundred more case report forms were shortly to be submitted to provide additional basis for a decision.

The question of the package insert was then raised and we pointed out that the package insert would have to present a well-rounded picture to the physician of just what had been accomplished in the clinical studies. It was suggested that tabulations would be required. The question was then asked whether this information had to be included in that part of the package insert which controlled medical advertising, since they felt that tabulations were difficult to insert in advertisements. We told them that we would contact our advertising department in an attempt to clarify the matter.

ROBERT O. KNOX, M.D.

MEMORANDUM

APRIL 25, 1969.

To: Peter G. James, Acting Chief, Statistical Analysis Branch.
From: Jacqueline M. Tillman, Statistical Assistant.
Subject: Statistical Review of NDA 16-618 (Ponderex) (vols. 3.1, 3.2 and 3.3).

I have examined the case records and summaries for 8 studies submitted by Dr. Robert Knox. These are listed below:

Study No.—Investigators name	Dates of study	Patients started
2002—John A. Owen, Jr.	Aug. 15, 1966 to Mar. 8, 1967	12
2009—Solomon Fisch, M.D.	Nov. 1964 to June 1967	60
2016—Benjamin A. Rosenberg, M.D., F.A.C.P.	Jan. 1965 to July 1967	34
2020—Robert S. Anderson, M.D.	Apr. 1965 to Nov. 1967	20
2025—Dorothy R. Hollingsworth, M.D.	Jan. 1966 to July 1967	25
2050-B—Martin S. Roginsky, M.D.	May 1966 to Apr. 1967	120
2055-B—George E. Bacon, M.D.	Oct. 1966 to Aug. 1967	20
2060—Sol B. Stern, Jr., M.D.	Aug. 1967 to Jan. 1968	37

The purpose of this review was to audit summary data submitted by the Firm (A. H. Robins Co.) and to assess generally the characteristics and validity of these studies and their raw data.

Despite a search of other NDA volumes and IND sources I have been unable to find a protocol for any of these studies. Thus we are unable to find an indication of study objectives, designs, data parameters and other factors pertinent to clinical and statistical review and labeling claims.

The only semblance of a protocol is the summary sheet(s) in Vol. 3.1 which accompanies the patient records for each of these studies.

In Study 2009 the Reference to Raw data sheet stated that it was a double-blind, randomized study. The drugs used were Fenfluramine capsules, 20 mg. and 40 mg., Dextroamphetamine 10 mg. and Placebo capsules. The results stated were Placebo weight loss per week—0.43 lbs., Fenfluramine 20 mg. weight loss per week—1.00 lbs., Fenfluramine 40 mg.—weight loss per week—0.54 lbs., and