We look forward to our discussion and thank you for your courtesy in making it possible.

Sincerely,

E. CLAIBORNE ROBINS.

Enclosure.

JANUARY 26, 1970
UPDATED JULY 6, 1970.

Subject: Fenfluramine Hydrochloride (NDA 16-618).

Fenfluramine hydrochloride is an appetite suppressant drug designed for use in the medical management of obesity. The A. H. Robins Company has licensed fenfluramine from Les Laboratoires Servier of France for sale in the United States, Canada and South America. It is presently marketed in France by Les Laboratoires Servier and in the United Kingdom by their subsidiary, Selpharm Laboratories, Ltd. In the United Kingdom it has received outstanding acceptance due to its lack of stimulating effect on the central nervous system. As in the United States, the British health authorities have been concerned about the stimulatory effect of amphetamines on the central nervous system and their consequent potential for abuse. This has resulted in the removal of all anti-obesity agents except fenfluramine from the list of drugs considered acceptable with respect to both safety and effectiveness for use under the National Health Service by the Standing Joint Committee on the Classification of Proprietary Preparations (Macgregor Committee.) Studies in the United States under the auspices of the A. H. Robins Company have confirmed the lack of stimulatory effect on the central nervous system and have demonstrated the effectiveness of this drug as an appetite suppressant.

All available European data and the results of animal safety studies conducted in the United States were submitted to the Food and Drug Administration with our Notice of Claimed Investigational Exemption for a New Drug in April 1964. The drug was then studied as an appetite suppressant in hospitals, clinics, and private practices throughout the country. As the reports from the physician investigators were received by our Medical Department, the data were tabulated and the effect of the drug on the weight of patients participating in weight reduction programs was analyzed by our medical and statistical departments. These analyses and the results of all studies in laboratory animals and human patients were submitted to the Food and Drug Administration in our New Drug Application dated March 3, 1967. This application contained data on 1,548 patients, over a thousand of whom received fenfluramine. The remainder received inert placebos or other available appetite suppressants in order that comparisons might be made with fenfluramine with respect to both effectiveness and safety.

The following is a chronology of the actions that have taken place since the submission of the New Drug Application:

March 8, 1967: FDA acknowledged receipt of NDA for fenfluramine.

August 31, 1967: FDA notified us that the application was incomplete in that it failed to contain adequate information concerning the synthesis, extraction, and purification of the new drug substance to determine its identity, strength, quality and purity. No additional animal or clinical data were requested.

September 20, 1967: Representatives of the A. H. Robins Company met with a chemist and medical officer of the FDA to discuss the chemical information requested in the FDA's letter of August 31, 1967 and the proposed labeling for the drug.

December 15, 1967: Information about the chemistry of fenfluramine and a revised package insert (labeling) were submitted to the FDA.

March 1, 1968: FDA chemist contacted to determine status of review. Between this date and June 7, 1968 numerous contacts with the Bureau of Medicine were made in an attempt to determine the reason for the continuing lack of response to our submission. Only vague excuses were offered.

June 7, 1968: Received phone call from Dr. Robert Hodges, Director, Office of New Drugs, who informed us that it had now been decided with Dr. Ley's concurrence that the application could not be approved until additional clinical data were submitted. This decision was prompted at least partally because most other drugs of this therapeutic class were then being reviewed for effectiveness by the NAS-NRC panels and reports had not then (and still have not) been implemented by FDA. It was felt by the FDA, therefore, that the application for fenfluramine should undergo an especially intensive review. This review resulted