Danowski, Professor of Medicine at the University of Pittsburg, Dr. Jay Tepperman, Professor of Medicine at the State University of New York at Syracuse, also a member of the Metabolic-Endocrine Committee, and Dr. H. J. Levin, a general practitioner, valued for his common-sense comments and careful opinions from the point of view of the day-to-day practice of medicine.

In addition to the clinicians, one or both of two statistical consultants were present at each meeting: Dr. Samuel Greenhouse and Mr. Jerome Cornfield, of the FDA Biometry Advisory Committee, Dr. Greenhouse being the Chairman of that Committee. The statisticians advised an interpretation of data, but did not make clinical recommendations.

The Consultants met twice, on June 27 and July 25. At the first meeting they studied the first results of the FDA review, acquainted themselves with background, format, and major decisions to be made and commented in preparation for the second meeting. In the latter meeting, consultants pored over data, drug by drug, and then drafted conclusions. Recommendations were drafted by the Chairman and Dr. Scoville in line with the conclusions and discussion of the meeting. These draft conclusions and recommendations were then mailed to the consultants for revision and concurrence. We have received letters from all four clinicians indicating concurrence (except for minimal editorial changes).

TAB D—DRAFT ANORECTIC DRUG LABELING: ACTIONS AND INDICATIONS

CLASS "ACTIONS" AND "INDICATIONS"

LABELING SECTIONS FOR ANORECTIC DRUGS

Actions.—Is a sympathomimetic amine with phamacologic activity similar to the prototype drugs of this class, the amphetamines. Actions include central nervous system stimulation and elevation of blood pressure. Tachyphylaxis and tolerance have been demonstrated with all drugs of this class in which these phenomena have been looked for.

Drugs of this class are commonly known as "anorectics" or "anorexigenus". It has not been established, however, that the action of such drugs in treating obesity is primarily one of appetite suppression. Other central nervous system actions, or metabolic effects may be involved, for example.

Adult obese subjects instructed in dietary management and treated with "anoretetic" drugs lose more weight on the average than those treated with placebo and diet, as determined in relatively shor-term clinical trials.

The magnitude of increased weight loss of drug-treated patients over placebo-treated patients is only a fraction of a pound a week. The rate of weight loss is greatest in the first weeks of therapy for both drug and placebo subjects and tends to decrease in succeeding weeks. The possible origins of the increased weight loss due to the various drug effects are not established. The amount of weight loss associated with the use of an "anorectic" drug varies from trial to trial, and the increased weight loss appears to be related [in part] to variables other than the drug prescribed, such as the physician-investigator, the population treated, and the diet prescribed. Studies do not permit conclusions as to the relative importance of the drug and non-drug factors on weight loss.

The natural history of obesity is measured in years, whereas the studies cited are restricted to a few weeks duration; thus, the total impact of drug-induced weight loss over that of diet alone must be considered clinically trivial.

Indication.—Is indicated in the management of exogenous obesity as a short term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class (see ACTIONS) should be measured against possible risk factors inherent in their use such as those described below.

TAB E—DRUG DEPENDENCE WARNING FOR ALL NON-AMPHETAMINE ANORECTICS EXCEPT FENFLURAMINE

Is related chemically and pharmacologically to the amphetamines. Amphetamines and related stimulant drugs have been extensively abused, and the possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines