10. A number of negative features in the NDA data will be reported in my subsequent, detailed report. However, there are two which cause some uneasiness. The first concerns the high dosage data for the placebo. The firm presents statistical summaries for each study showing the high dosage incrementation over the 12 week study period. It fails to show similar data upon which to determine whether the high dosage placebo was incremented in the same manner. The implications may be minor, but could be major.

11. The other negative feature concerns the range of efficacy which may be attributed to the drug products. It is the small number of subjects in each study and in all studies combined upon which to base claims for efficacy. Should these claims be extended to the different dosage regimens and to the male/female sub-groups the supporting study data becomes increasingly sparse, even when all studies are combined. One investigator failed to get any males into his study. Others had no more than a sole male patient in one or more of the drug or placebo regimen groups. Some studies did not have critical drug to placebo comparisons for males thus failing to provide support for "well-controlled clinical trials".

12. Of critical import is the fact that the better results of the studies, overall, were observed in the male groups. However, even should all complete studies be combined the number of males is 10 and 15 in the high and fixed drug dosage groups and 13 and 11 in the respective placebo groups. This paucity of male subjects was mentioned to you, orally; however, its significance was discounted because this appeared to be "representative". The concept of "representativeness" may have been misconstrued. It was not the purpose of these studies to enter patients in such a manner as to represent the proportion of overweight males and females motivated to lose weight. It was the purpose to get enough males to determine the drug regimens' relative effectiveness.

13. At this point the sufficiency of data for males is borderline if we combine all studies and both regimens. It probably is not sufficient to support claims for either drug dosage regimen.

MEDICAL OFFICER'S REVIEW OF NDA 16-618

Product: "Pondimin".
Sponsor: A. H. Robins Co., Richmond, Va.
Date of Submission: Mar. 25, 1970.

Firm submits draft labeling for package insert for NDA 16-618 based on our conference with the firm on March 23, 1970.

Labeling review

Firm has made all the revisions recommended in our conference with them on March 23, 1970.

Clinical references have been reviewed and are considered satisfactory.

The labeling has been compared to the guidelines for "Anorectic Preparations" prepared by OMD and is considered acceptable.

Conclusion

The application is complete and approval is recommended.

JAMES M. MOSER, Jr., M.D.,
Division of Neuropharmacological Drugs.

A. H. ROBINS CO.,
Richmond, Va., July 9, 1970.

CHARLES E. EDWARDS, M.D.,
Commissioner, Food and Drug Administration,
Department of Health, Education and Welfare,
Rockville, Md.

DEAR COMMISSIONER EDWARDS: I appreciate your willingness to meet with representatives of Robins and Congressman Satterfield to discuss the Company's National Drug Act 16-618 for fenfluramine hydrochloride. Mr. Satterfield has advised us that the meeting is scheduled for 2 p.m., Tuesday, July 14, 1970, at: Federal Office Building #8, 200 "C" Street, Room 6819, Washington, D.C.

In order to permit a more meaningful exchange, I enclose for your prior review a history of NDA 16-618. Although prepared internally, objectivity was the goal in the preparation of this history.