MEMORANDUM

NOVEMBER 18, 1969.

To: John Jennings, M.D., Acting Director, Bureau of Medicine.
From: Robert O. Knox, M.D., DND/OND/MED.
Subject: Pending class labeling for anorexigenics.

I would like to draw your attention to the fact that there is now pending a class labeling for anorexigenics. This class labeling is under consideration for publication in the Federal Register in the near future. This labeling may lead the physician to erroneously conclude that anorexigenics are more effective than they actually are. The labeling of these drugs in the past has been misleading as far as efficacy is concerned. Would it not be desirable to include in the class labeling a factual statement as to the actual amount of weight loss achieved in the studies submitted in support of any given NDA?

The promotion of Pro-Sate is typical in that it gives results in terms of the amount of weight loss *per week* without giving any idea of the total number of pounds lost or the duration of treatment. Most of the studies submitted in behalf of anorexigenics run from one to two months or less. The dissenting minority opinion of the NRC/NAS panel evaluated the sympatho-mimetic stimulants as "probably effective" as anorexiants. Their reasoning for the "probably effective" evaluation was that:

(a) Most studies of the preparations have been for short periods;

(b) There is no available evidence that the use of these anorexiant preparations alters the natural history of obesity;

(c) There is some evidence that anorectic effects may be strongly influenced by the suggestibility of the patient, and

(d) There are reservations about the adequacy of the controls in some of the clinical studies. The minority suggested that controlled studies on the long-term anorectic efficacy of the sympatho-mimetic stimulants be conducted.

Although there may be no precedent for this type of package insert, these drugs fall into a special category as far as efficacy and abuse are concerned.

Enclosed is a copy of my memorandum dated May 19, 1969 concerning the establishment of an FDA policy regarding anorexigenics.

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MEMORANDUM

FEBRUARY 17, 1970.

To: John Jennings, M.D., Acting Director, Bureau of Medicine.
From: Robert O. Knox, M.D., DND/OND, MD 120.
Subject: Position paper on FDA policy concerning the labeling of amphetamines and amphetamine-like compounds.

*References.*—(1) My memo to Dr. Gibson dated May 10, 1969. (2) My memo to Dr. Jennings dated November 18, 1969.

1. I discussed labeling for the amphetamines with representatives of the Office of Marketed Drugs; however, we were unable to agree on the proper wording for the package inserts for these drugs.

2. Therefore, I am summarizing my thoughts on this matter as follows:

A. It is generally agreed that there is a definite danger of abuse connected with the use of these drugs.

B. While there is no unanimity of opinion as to the efficacy of these drugs, the following opinions merit careful consideration:

(a) The British Medical Association has concluded that "These drugs should be avoided so far as possible in the treatment of obesity . . ."

(b) Arthur Grollman has stated that ". . . There is no evidence to indicate that these agents suppress appetite as has been claimed, which is the basis usually for advocating their use. The only rationale for their use is the hope that by counteracting the depression induced by hunger the patient is better able to abstain from overeating. However, the anorexigenic agents have proven of little efficacy in actual practice . . ." (Pharmacology & Therapeutics, Lea and Febiger, 1965.)

(c) Feinstein, A. R., J. Chr. Dis. 11:349–389, No. 4, April 1960. ". . . The results obtained with anorexiant agents therefore (1) are in many instances inferior to those obtained with unsupplemented diets, (2) show the same marked variations present in the tabulated results of diet alone, and (3)