4. That single-entity oral "anorectic" preparations including the amphetamines be permitted to be labeled for restricted use in obesity provided that they are used in association with a specific weight reduction program and that the clinically trivial contribution of these drugs to the overall weight reduction is properly emphasized. To carry out the latter recommendation a statement such as that made in the conclusions drawn from this review must be included in all labeling and promotional products. This statement should include the following points:

Studies of the effect of "anorectic" drugs in the treatment of obesity when compared with the effects on patients treated in a similar manner without the use of the drugs demonstrate that the magntiude of weight loss of drug treated patients over non-drug treated patients was only a fraction of a pound a week. The rate of weight loss was greatest in the first weeks of study for both the drug and the non-drug treated subjects and tended to decrease in succeeding weeks. The natural history of obesity is measured in years whereas the studies offered for review 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. The limited usefulness of these agents must be measured against any possible risk factors such as nervousness, insomnia and drug habituation that might be inherent in their use. Moreover, these agents can only be recommended for use in the treatment of obesity in a carefully monitored and specified weight reduction program under the care of a physician.

5. That future approval of all "anorectic" drugs prepared for future use be based on demonstration of efficacy as measured by statistical superiority of the drug over placebo in trial using FDA recommended protocols. These protocols should include provisions, among others, for the testing of a specific target population, specification of a minimum duration trial to assure clinical relevance of the study and give consideration to the handling of patient drop-out.

6. Further, that appropriate summary data derived from efficacy studies be presented in labeling and in all promotional material to indicate the degree of weight loss that was found. For this purpose the guidelines noted in (4) above should be supplemented by the addition of the specific facts found for the specific drug under consideration.

MAY 6, 1976.

Since the Panel discussions on January 18, 1976 and March 16, 1976 reveal that the Panel members were not fully conversant with the manner in which the computer analysis of the 206 anorectic studies was carried out, and since the remarks of the Executive Secretary and the Chairman (see transcripts of January 18, 1976, pages 138–153, and March 16, 1976, pages 13–15) may have given the Panel members a very erroneous impression of the nature of this computer analysis and of how it was subsequently used by the outside consultants, I would like to draw the Panel's attention to the following:

1. An undated Action Memorandum,[1] concerning the FDA's posture on the anorectics, from Dr. Crout to Dr. Simmons, contains, as Attachment A, an FDA Drug Bulletin draft which states on page 2:

"* * * After initial screening and review by six physician-medical officers records of 206 drug trials were found adequate for in-depth analysis."

These six physicians were asked to give their opinions as to whether each of the studies they reviewed was adequate to permit valid conclusions. (One of the Study Description sheets is attached.) Of the 206 studies reviewed, 122 were contained in just three NDAs. As can be seen from the following tabulation derived from data accumulated by FDA statisticians, the reviewing physicians deemed less than half of the 122 to be adequate to permit valid conclusions:

NDA No.: Name of drug	Reviewing physician	Does study permit valid conclusions?			Total
		Yes	No	Uncertain	
16–618: Pondimin	Dr. Freeman	0	21	0	21
	Dr. Wright	0	16	0	16
16–880: Voranil	Dr. Trilling	33	18	3	54
17–247: Mazindol	Dr. Woo	16	6	9	31
Total		49	61	12	122

[1] Which was followed by an Action Memorandum, dated October 6, 1972, from Dr. Simmons to then Commissioner Edwards.