April 6, 1971.—Panel on Anorexigenic Drugs. The Chairman (1) takes the position that:

(a) all that was needed was a demonstration of a statistically significant difference between placebo and active drug. I object that this is an inadequate method of determining efficacy because the amount of weight loss needed to demonstrate a statistically significant difference becomes smaller as the number of patients entered into the study increases.

(b) 12 weeks was the minimum duration of therapy that would provide meaningful data. (27–A, 27–B)

April 19, 1971.—Supervisory MO (m), DNDP, memo (27–D) to Deputy Director, BuDrugs, states that in his opinion 4–8 weeks is entirely satisfactory for anti-obesity studies and that there is no scientific rationale for 12-week studies. (Cf. Federal Register statement of 8–8–70 above).

(*Volume 5.1*)

August 31, 1971.—Sponsor submits 66 more volumes. (12)

September 13–14, 1971.—Second Advisory Panel Meeting on Anorexigenics. (27–F) The previous position, that only a statistically significant difference was needed to show efficacy, is relinquished.[7]

November 8, 1971.—The Deputy Director for Scientific Activities phones me to tell me to report on "*detail*" the following morning to the Division of Oncology and Radiopharmaceuticals (DOR). No "Notice of Personnel Action" was received by me. On reporting to DOR, 11–9–71, I find that office space is not immediately available for me, hence I return to DNDP and continue to work there until an office becomes available, a week or so later.[8]

March 12, 1972.—Letter from Director (k) DNDP to sponsor advises that: " . . . In view of unusual Public Health problems as well as considerations relating to the efficacy of anorectic agents we have found it necessary to develop special criteria and procedures for the review and evaluation of the safety and efficacy of anorectic agents." (29)

June 12–13, 1972.—A meeting was held in Washington, D.C. to "discuss the medical and social issues of amphetamines and related compounds in managing obesity. . . ." (See Section 9)

June 27 & July 25, 1972.—Consultants on Anorectic Drugs meet "to review data just compiled by FDA staff on the safety and efficacy of anorectic drugs." One of their recommendations is that approval of "anorectic" drugs be based on demonstration of efficacy as measured by statistical superiority of the drug over placebo. (30; para. 5)[9]

Efficacy is not defined; the duration of the trials is not specified.

October 6, 1972.—Memo (32) from Bureau Director (e) to Commissioner recommends that judgments on the efficacy of anorectic drugs be based "on the currently available substantial evidence derived from short-term studies . . ."

January 10, 1973.—Grounds for Approvable Letter (33), based on the "Amphetamine-Anorectic Review Project" (AARP), prepared by Deputy Director (u), DNDP.

February 15, 1973.—FDA issues "approvable" letter. (34)

(*Volume 6.1*)

May 1, 1973.—FDA letter requests revision of Drug Dependence section to include reports of abuse (80 to 400 mg) associated with euphoria, derealization and perceptual changes. (35)

June 14, 1973.—FDA issues approval letter. (36) The package insert does not contain any tabulations of the amount of weight loss; the wording of the Consultants' Statement, ". . . the total impact of drug-induced weight loss over that of diet alone must be considered clinically trivial . . .," has been altered to read: ". . . clinically limited." (37)

June 18, 1973—Competitor claims fenfluramine has been suggested to cause risk of serious abuse in Scotland, S. Africa, and Jamaica. (See BNDD statement, Federal Register 38, No. 89, 5–9–73). (38)

---

[7] Minutes of this meeting are unavailable.

[8] On August 21, 1972, a "Notification of Personnel Action" dated 03–31–72 is delivered to my office notifying me that I had been transferred to DOR. (28)

[9] This is an attachment ("TAB C") to an undated, 21-page, memo from Acting Director (o), OSE, to Director, BuDrugs.