When the BuMed was reorganized in 1966, the anorexiants were assigned to the Division of Neuropharmacologic Drug Products (DNDP) and I was transferred at my request to that Division in order to continue working on the same types of NDAs, e.g., anorexiants.

2. ABBREVIATED RESUME OF NDA 16-618. (FOR FULLER CHRONOLOGY, SEE SECTION 3)

March 3, 1967.—NDA 16-618, Ponderex (Pondimin, fenfluramine) received by FDA.

June 20, 1968.—BuMed issues an "inadequate" (not approvable) letter.

November 4, 1968.—14 more volumes added to NDA.

May 6, 1969.—My Medical Officer Review (MOR) recommends nonapproval.

May 11, 1969.—Sponsor accuses me of bias.

September 9, 1969.—I drafted a non-approval letter to be sent to the sponsor. This rough draft listed a number of serious discrepancies.

October 2, 1969.—NDA 16-618 was removed from my office without prior notification or explanation and reassigned to a third Medical Officer (MO).

October 23, 1969.—The third MO concludes that the NDA was not approvable.

November 25, 1969.—9 more volumes were submitted containing 9 additional studies.

December 29, 1969.—The third MO concludes in his second MOR that the data is adequate to support an appetite suppressant claim. He made no mention of the amount of weight lost. When I, belatedly, obtained a copy of the December 29, 1969, MOR, I advised the Division Director, and then the Bureau Director, of my concern regarding the lack of quantitative data in this MOR.

The "approvable" letter which had been drafted for signature by the Bureau Director did not issue.

May 21, 1970.—I found in the Division files a revised MOR, also dated December 29, 1969, which had been altered to include a sentence to the effect that a weight loss of 5 lbs. was considered satisfactory evidence of effectiveness.

June 24, 1970.—The Director of DNDP is replaced by a second Director who reassigned the NDA to a fourth MO.

August 6, 1970.—MOR concludes that the November 25, 1969 studies are inadequate individually and collectively to establish anorexigenic efficacy.

September 11, 1970.—An "inadequate" letter issued by BuDrugs.

April 6, 1971.—An Advisory Panel took the position that a statistically significant difference between placebo and drug was all that was necessary to justify approval of an anorexiant. I objected to this.

August 31, 1971.—66 more volumes added to NDA.

September 13-14, 1971.—The Second Advisory Panel altered its previous position re statistical significance.

November 8, 1971.—I was transferred on less than 24-hr. notice from the DNDP to the Division of Oncology and Radiopharmaceuticals (DOR).

About this time, the BuDrugs arranged for a computer analysis of 206 studies, all of which had been conducted on behalf of various drug firms over a period of 12 years, to be carried out by the Statistical Division. "The statisticians advised an interpretation of data, but did not make clinical recommendations." After considering this statistical analysis the Panel concluded, in 1972, that the amount of weight loss induced by anorexiants was "clinically trivial." In spite of this, the BuDrugs, in 1973, issued approval letters for several anorexiants. The package insert did not contain any tabulation of the amount of weight loss achieved, but merely stated that weight loss was "clinically limited."

3. EXPANDED CHRONOLOGY OF NDA 16-618

(*Volume 1.1*)

March 3, 1967.—A. H. Robins submits NDA 16-618, consisting of 22 volumes, for fenfluramine, which was claimed to have a marked advantage over amphetamine in that it was non-stimulating and therefore unlikely to cause abuse. The NDA is assigned for review to a Public Health intern (a)[2] in DNDP.

July 28, 1967.—I write a memo to the Division Director, DNDP (5) recommending revision of the package insert for "anorexigenics."

August 29, 1967.—MOR, written by a PHS Intern, states: "... the claim that drug is an anorexic indicated an adjunctive therapy would appear to be supported." (6)

[2] Letters in parentheses refer to names of persons referred to in the text. See Key in Section 5.