well-controlled trials that patients taking the drug sustain a statistically significant greater degree of weight loss than patients taking a placebo. While it would obviously be of value to know with certainty the effect of the drug on the natural history of the disease, we have considered this to be a public health question which an individual drug firm cannot reasonably be expected to answer in the context of evaluating its particular product.

The approach taken in conducting the anorectic review was discussed by Dr. Henry E. Simmons, the former Director of the Bureau of Drugs, in his testimony before this subcommittee on December 13, 1972, and I would like to restate his description of its magnitude:

> The scope of the program was ambitious, and involved over 1,000 volumes of data concerned with twelve single entities. The drug products in which these entities were present, either alone or in combination, were marketed by 40 firms. Over 200 double-blind and controlled studies of efficacy which had been carried out on almost 10,000 subjects were included in the review.
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> Individual patient data sheets were coded and key punched to facilitate computer analysis. This produced over 70,000 computer cards, representing over 70,000 patient visits of the 10,000 subjects. Each card included certain patient characteristics as well as changes in weight, blood pressure, pulse, and other possible adverse effects from visit to visit. The cards contained over 4 million units of information. Programs were then written to permit automatic statistical analysis in order to determine what effect the active drug had when compared with the placebo under "double-blind" controlled conditions.

These studies were then evaluated by our medical staff to determine whether there was, for each drug entity, substantial evidence that patients taking the drug sustained on the average a greater degree of weight loss over a 12-week period than patients on a placebo. The 12-week period was selected because it was the longest period for which there was reasonably comparable data on all of the drug entities in the review.

The results of this review were presented to FDA consultants during two meetings in 1972. This group was chaired by Dr. Thaddeus E. Prout, professor of medicine at Johns Hopkins University School of Medicine. Their recommendations were, among others, as follows:

1. The single-entity anorectic drugs including the amphetamines should "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."
2. The future approval of anorectic drugs should be "based on demonstration of efficacy or measured by statistical superiority of the drug over placebo in trials using FDA recommended protocols." The group did not recommend that demonstration of a long-term effect on the natural history of obesity be necessary for marketing.
3. All drugs in the anorectic class except fenfluramine should "be placed in schedule II on the basis of abuse potential."

As a result of this review, the following actions were taken by FDA in 1972–73:

1. FDA required that the anorectic drugs be relabeled to emphasize necessary warning information about their potential for abuse, and also to reflect accurately the indications for which they