

In 1972 the Food and Drug Administration carried out an overall review of all drugs used in the treatment of obesity. The FDA concluded that all drugs used in treating obesity or proposed for treating obesity did indeed possess some abuse potential; the control of the remaining drugs was finally achieved in 1973. (The drugs placed under control were as follows: phendimetrazine (Plegine), benzphetamine (Didrex), chlorphentermine (Pre-Sate), mazindole (Sanorex), clor-termine (Voramil), all in Schedule III and fenfluramine (Pondimin), diethylpropion (Tenuate), and phentermine (Ionamin), into Schedule IV, the latter two in IV only because the manufacturer petitioned for a hearing—they had been recommended for Schedule III).

The changes in scheduling have had an interesting, differential effect. Schedule II prohibits refilling of prescriptions, and allows the Justice Department to impose production quotas that are based in large part on HEW estimates of medical and scientific needs. Schedules III and IV allow five refills of prescriptions in six months time, and do not impose production quotas. The impact of imposing Schedule II controls resulted in a drastic decrease in the distribution of amphetamines following the transfer of these drugs from Schedule III into Schedule II. Monthly pharmacy prescriptions dropped from between one and a half million to two million per month to approximately six hundred and fifty thousand prescriptions per month. There has been an additional continuing downward trend; on the basis of the downward trend together with the elimination of certain combination and injectable amphetamine products, the Bureau of Narcotics and Dangerous Drugs, utilizing FDA recommendations, has now imposed quotas permitting only approximately 8% of the amphetamines production which existed prior to rescheduling. The rescheduling of drugs into Schedules III and IV has not so far produced a decrease in prescriptions for these drugs.

TABLE B—DRAFT PREAMBLE TO PROPOSE ANORECTIC SPI

The Food and Drug Administration has reviewed extensive data on "anorectic" drugs used in obesity and concludes that the drugs have a limited place in obesity treatment regimens. The Agency concluded that all of the drugs investigated possess some potential for abuse and so should be used with particular care. The most controversial members of the therapeutic class, the amphetamines, produce weight loss, too, and so will continue to be labeled for use in obesity. The Agency will continue to check all evidence of non-therapeutic use and diversion through prescription abuse; if present control measures prove inadequate during the next year, further restrictions will be necessary.

These decisions were made following a review of seven months time of the over 200 controlled, double-blind studies submitted to the Agency in the last 12 years by manufacturers of anorectic drugs. These include a number of amphetamine preparations such as Dexedrine, Biphedrine, and Obotan, and closely related congeners, such as phenmetrazine (Preludin), methamphetamine (Syndrox, Desoxyn), benzphetamine (Didrex), phendimetrazine (Plegine), diethylpropion (Tenuate, Tepanil), phentermine (Ionamin, Wilpo), and chlorphentermine (Pre-Sate). In addition, studies carried out with three as yet unmarketed drugs were also reviewed and indicated that these drugs are basically comparable with older agents. They will thus probably be approved for marketing after technical details are ironed out.

The FDA relied in part on the advice of a task force of outside consultants, chaired by Dr. Thaddeus E. Prout of Johns Hopkins. Consultants and FDA agreed that the risks of parenteral injections of amphetamines outweighed any possible advantages associated with these routes of administration, so that "anorectic" drugs will be marketed only for use by the oral route.

Data were also reviewed on the efficacy of combination drugs, chiefly on the possible role of barbiturates or tranquilizers in counteracting the adverse effects of the principal active agents. The combinations generally were found not to differ in a statistically significant way either in efficacy or in the incidence of adverse side effects.

The review project made unique use of the massive files of data in FDA to obtain a computerized overview of the whole therapeutic class. After initial screening and review by six physician-medical officers, records of 206 drug trials were found adequate for in-depth analysis. Individual patient records including patient characteristics, treatments, serial weights, dates of all visits, and any