BUREAU OF NARCOTICS & DANGEROUS DRUGS

Attachment A

(Reprinted from Federal Register of February 12, 1973; 38 F.R. 4249)

Title 21—Food and Drugs

CHAPTER I—FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

SUBCHAPTER C—DRUGS

PART 130—NEW DRUGS

Amphetamines for Human Use

On August 8, 1970, there was published in the FEDERAL REGISTER (35 FR 12652) § 130.46 concerning amphetamines and their salts and levamfetamine and its salts. Section 130.46 required the submission of new drug applications for amphetamine or dextroamphetamine and their salts as a condition for continued marketing. The new drug applications were to contain evidence of efficacy, including efficacy in the treatment of obesity.

Pursuant to that requirement 106 new drug applications for amphetamines or amphetamine-containing drugs were received. The analysis of the data submitted concerning the amphetamines and other, nonamphetamine anorectic drugs generally supported the efficacy of anorectic drugs. Use of the drug in obese patients was associated with more weight loss than was diet alone. The degree of extra weight loss was small (a few tenths of a pound a week in many cases), variations were great, and the rate of weight loss decreased after the first weeks of therapy.

On the basis of the currently available evidence, the Commissioner concludes that oral dosage forms of amphetamine and/or dextroamphetamine are effective in the management of exogenous obesity as a short term (a few weeks) adjunct in a regimen of weight reduction based on calorie restriction for patients in whom obesity is refractory to other measures. Appropriate notices concerning such drugs which have been reviewed in the Drug Efficacy Study will be published in the FEDERAL REGISTER.

Use of amphetamines for long periods of time may lead to drug dependence and abuse. Abuse of the amphetamines has been well known. Persistence of abuse under conditions of marketing described herein may lead the Commissioner to take further steps to restrict the use of these drugs.

No data have been received providing substantial evidence of effectiveness of levamfetamine and its salts. Accordingly these preparations continue to be regarded as new drugs requiring approved full new drug applications.

On September 3, 1971, a Drug Efficacy Study Implementation notice was published in the FEDERAL REGISTER (36 FR 17667) stating that methamphetamine hydrochloride injection (intended for other than anorectic indications) was regarded as effective for some indications and less than effective for others. The Commissioner has now fully reviewed the evidence on the safety and effectiveness of this drug, and has concluded that the well-documented history of abuse of parenteral methamphetamine, together with the severe risk of dependence and the availability of safer and equally effective alternative drugs, creates an unfavorable balance of risk to benefit. A proposal to withdraw approval of these new drug applications as lacking evidence of safety is published elsewhere in this issue of the FEDERAL REGISTER. The Commissioner also concludes that, for the same reasons, parenteral preparations containing amphetamine, dextroamphetamine, or levamfetamine or their salts are lacking evidence of safety.

On August 8, 1970, a Drug Efficacy Study Implementation notice was published in the FEDERAL REGISTER (35 FR 12678) stating that various combination drugs containing an anorectic drug were regarded as possibly effective for their claimed anorectic effects and lacking substantial evidence of effectiveness for their other indications. Data were received concerning those drugs and also combination drugs which were subjects of new drug applications submitted as required by § 130.46. The combinations consisted of anorectic agents associated with, for example, sedatives, tranquilizers, rauwolfia derivatives, or vitamins. The data were reviewed and found not to fulfill the criteria set forth in the Statement of General Policy or Interpretation § 3.85 Fixed-combination prescription drugs for humans, published in the FEDERAL REGISTER of October 15, 1971 (36 FR 20037). Further, in view of the lack of substantial evidence of effectiveness of the drugs as fixed combinations, the recognized potential for abuse of the amphetamine, dextroamphetamine, methamphetamine, and phenmetrazine components, and the availability of alternative therapeutic measures which are safer and effective, combinations containing such components also lack proof of safety. Proceedings to withdraw approval of such applications are being initiated, and an appropriate notice is published elsewhere in this issue of the FEDERAL REGISTER.

In a forthcoming issue of the FEDERAL REGISTER, the Commissioner will set forth his policy with respect to anorectic agents in general.

On the basis of all of the data and information submitted pursuant to § 130.46, pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (secs. 502 (f), (j), 505, 701(a), 52 Stat. 1051-53; as amended, 1055; 21 U.S.C. 352(f), (j), 355, 371(a)), and under the authority delegated to him (21 CFR 2.120), the Commissioner of Food and Drugs hereby revises § 130.46 of Part 130, Subpart A to read as follows:

§ 130.46 Amphetamines (amphetamine, dextroamphetamine, and their salts and levamfetamine and its salts) for human use.

(a) Amphetamine and dextroamphetamine and their salts. (1) Pursuant to the drug efficacy requirements of the Federal Food, Drug, and Cosmetic Act, the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, has evaluated certain dosage forms of amphetamines and other sympathomimetic stimulant drugs intended for use in the treatment of obesity and for other uses. The Academy found that such drugs as a class have been shown to have a generally short-term anorectic action. They further commented that clinical opinion on the contribution of the sympathomimetic stimulants in a weight reduction program varies widely, the anorectic effect of these drugs often plateaus or diminishes after a few weeks, most studies of them are for short periods, no available evidence shows that use of anorectic alters the natural history of obesity, some evidence indicates that anorectic effects may be strongly influenced by the suggestibility of the patient, and reservations exist about the adequacy of the controls in some of the clinical studies. Their significant potential for drug abuse was also cited.

(2) In addition to those dosage forms that were reviewed for efficacy by the Academy, other dosage forms of amphetamine drugs are on the market that were not cleared through the new-drug procedures. While certain amphetamines were marketed prior to enactment of the Federal Food, Drug, and Cosmetic Act in 1938, some of the conditions of use subsequently prescribed, recommended, or suggested in their labeling (for example, for the treatment of obesity) differ from uses claimed for the amphetamines before said enactment. Such uses