

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 (35 FR 17669) 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 those 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 § 3.86 Fixed-combination prescription drugs for humans, published in the Federal Register of October 13, 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 (sec. 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