DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 95D–0349]

Immediate Release Solid Oral Dosage Forms; Scale-Up and Postapproval Changes: Chemistry, Manufacturing, and Controls; In Vitro Dissolution Testing; In Vivo Bioequivalence Documentation; Guidance

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is publishing a guidance entitled ''Immediate Release Solid Oral Dosage Forms; Scale-Up and Postapproval Changes: Chemistry, Manufacturing, and Controls; In Vitro Dissolution Testing; In Vivo Bioequivalence Documentation.'' The guidance sets forth application information that should be provided to the Center for Drug Evaluation and Research (CDER) to assure continuing product quality and performance characteristics of immediate release solid oral dose formulations for specified changes. The guidance fulfills a commitment made in the President's National Performance report, ''Reinventing Drug and Medical Device Regulations,'' April 1995, to reduce through guidance the number of manufacturing changes that require preapproval by FDA. The guidance provides recommendations to sponsors of new drug applications (NDA's), abbreviated antibiotic applications (AADA's), and abbreviated new drug applications (ANDA's) who intend, during the postapproval period, to change the components or composition of the drug, site of manufacture, scale-up/scale-down of manufacture, and/or manufacturing process or equipment. The guidance was prepared by the Immediate Release Scale-Up and Postapproval Change Expert Working Group of the Chemistry Manufacturing Controls Coordinating Committee (CMC CC) at CDER.

DATES: Written comments may be submitted at any time.

ADDRESSES: Submit written requests for single copies of the guidance ''Immediate Release Solid Oral Dosage Forms; Scale-Up and Postapproval Changes: Chemistry, Manufacturing, and Controls; In Vitro Dissolution Testing; In Vivo Bioequivalence Documentation'' to the Consumer Affairs Branch (HFD–8) (previously the CDER Executive Secretariat Staff), Center for Drug Evaluation and Research, Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855. Send two self-addressed adhesive labels to assist that office in processing your requests. An electronic version of the guidance document is also available via Internet. Requesting persons should connect to the CDER FTP server (CDVS2.CDER.FDA.GOV) using the FTP protocol. The guidance is available in WordPerfect Versions 5.2 and 6.0. Submit written comments on the guidance to the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20857. Requests and comments should be identified with the docket number found in brackets in the heading of this document. A copy of the guidance and received comments are available for public examination in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

FOR FURTHER INFORMATION CONTACT: Allen Rudman, Center for Drug Evaluation and Research (HFD–645), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301–594–0375.

SUPPLEMENTARY INFORMATION: FDA is publishing a guidance entitled ''Immediate Release Solid Oral Dosage Forms; Scale-Up and Postapproval Changes: Chemistry, Manufacturing, and Controls; In Vitro Dissolution Testing; In Vivo Bioequivalence Documentation.'' The guidance specifies application information that sponsors should provide to CDER to assure continuing product quality and performance characteristics of immediate release solid oral dose formulations for changes made in NDA's, AADA's, and ANDA's. The guidance fulfills a commitment made in the President's National Performance report, ''Reinventing Drug and Medical Device Regulations,'' April 1995, to reduce through guidance the number of manufacturing changes that require preapproval by FDA.

The guidance is the result of: (1) A workshop on the scale-up of immediate release drug products conducted by the American Association of Pharmaceutical Scientists in conjunction with the United States Pharmacopoeial Convention and FDA; (2) research conducted by the University of Maryland at Baltimore on the chemistry, manufacturing, and controls of immediate release drug products under the FDA/University of Maryland Manufacturing Research Contract; (3) the drug categorization research conducted at the University of Michigan and the University of Uppsala on the permeability of drug substances; and (4) the Scale-Up and Post Approval Changes (SUPAC) Task Force which was established by the Center for Drug Evaluation and Research Chemistry, Manufacturing, and Controls Coordinating Committee to develop guidance on scale-up and other postapproval changes.

The guidance describes: (1) The levels of change that may be made in the components or composition of the drug, site of manufacture, scale-up/scale-down of manufacture, and manufacturing process and equipment; (2) the chemistry, manufacturing, and controls tests for each level of change; (3) in vitro dissolution tests and/or in vivo bioequivalence tests for each level of change; and (4) filing documentation.

The regulations in § 314.70(a) (21 CFR 314.70(a)) state that applicants may make changes to an approved application in accordance with a guideline, notice, or regulation published in the Federal Register that provides for a less burdensome notification of the change (for example, by notification at the time a supplement is submitted or in the next annual report). This guidance permits less burdensome notice of certain postapproval changes within the meaning of § 314.70(a).

For postapproval changes for immediate release dosage forms that affect components and composition, scale-up, site change, and manufacturing process or equipment changes, this guidance supersedes the recommendations in section 4.G of the Office of Generic Drugs Policy and Procedure Guide 22–90 (September 11, 1990). For all other dosage forms and changes, this guidance does not affect the recommendations in Guide 22–90.

This guidance is an informal communication under 21 CFR 10.90(b)(9) that reflects the best judgment of CDER employees at this time. It does not create or confer any rights, privileges, or benefits for or on behalf of any person, nor does it operate to bind or obligate FDA in any way. Different approaches may be followed, but the applicant is encouraged to discuss significant variations in advance with FDA review divisions to preclude spending time and effort in preparing a submission that FDA may later determine to be unacceptable.

Interested persons may, at any time, submit written comments on the guidance to the Dockets Management Branch (address above). Two copies of any comments are to be submitted, except that individuals may submit one