the contact person listed below. Interested persons may submit data, information, or views on this subject to the Dockets Management Branch (address below).

ADDRESSES: The public workshop will be held at the Parklawn Bldg., conference rooms G and H, 5600 Fishers Lane, Rockville, MD 20857, Written data, information, or views regarding the workshop may be submitted to the Dockets Management Branch (HFA-305), Food and Drug Administration, rm. 1-23, 12420 Parklawn Dr., Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: John W. Levchuk, Center for Drug Evaluation and Research (HFD-322), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301-594-0095.

SUPPLEMENTARY INFORMATION:

I. Background

PET is a diagnostic imaging modality consisting of onsite production of radionuclides that are usually intravenously injected into patients for diagnostic purposes. The potential usefulness of a PET radiopharmaceutical is based upon the product's interaction with a biochemical process in the body. For example, the product may be substituted for glucose in anaerobic glycolysis, theoretically localizing in ischemic tissues (epileptic foci, acute vascular insufficiency states) where glucose metabolism is the predominant energy source.

The manufacture of PET radiopharmaceuticals consists of a process that takes place within a few hours. A target material is irradiated in a cyclotron; chemical synthesis takes place in a programmed, automated apparatus; and the final solution is prepared. The biological distribution of a PET radiopharmaceutical in the body is monitored by a positron tomograph, or PET scanner, which detects the photons emitted as a result of the radioactive decay of the PET radiopharmaceutical.

Currently, there are two FDA approved PET radiopharmaceuticals: Rubidium-82 (rubidium chloride ([82Rb]RbCl)) and fludeoxyglucose (18-F-FDG). At present, most investigational PET radionuclides are manufactured by cyclotrons at PET facilities, which generally are located at major teaching hospitals or their adjacent universities. Because PET radiopharmaceuticals contain positron emitting isotopes that have relatively short half-lives (minutes to hours), they are manufactured near the site of administration to patients. Products may be distributed to other institutions when the geographic

proximity of these locations will allow for distribution and use within the product's half-life parameters.

The development of PET radiopharmaceuticals has increased considerably over the past several years. As this technology has advanced, questions have been raised about the most appropriate approach to regulation of PET radiopharmaceuticals. FDA held a public hearing on March 5, 1993, to receive information and views on this issue from interested groups and individuals. The docket established for the receipt of comments (Docket No. 93N-0005) remained open for an additional 2 weeks after the hearing. Additionally, FDA has received several citizen petitions on PET radiopharmaceuticals to which it will be directly responding.

Having considered the available information, including that presented to the agency at the hearing and in written materials, FDA has concluded that radiopharmaceuticals should be regulated under the drug provisions of the Federal Food, Drug, and Cosmetic Act (the act). Under section 501(a)(2)(B) of the act (21 U.S.C. 351(a)(2)(B)), drugs are considered adulterated unless manufactured in conformity with current good manufacturing practice (CGMP). Because of unique features of PET radiopharmaceuticals, the applicability of certain requirements in the CGMP regulations for finished pharmaceuticals (part 211 (21 CFR part 211)) to PET radiopharmaceuticals may differ from the applicability of these requirements to drugs produced through traditional manufacturing methods. Consequently, elsewhere in this issue of the Federal Register, FDA is publishing a proposed rule that would authorize the Director of the Center for Drug Evaluation and Research (CDER) or the Director of the Office of Compliance, CDER, to approve exceptions or alternatives to the application of the provisions of part 211 to the manufacture of PET radiopharmaceuticals.

In order to assist manufacturers in complying withapplicable CGMP requirements, FDA has also developed a "Draft Guideline on the Manufacture of Positron Emission Tomographic (PET) Drug Products." A notice of availability of this draft guideline, on which the agency is inviting comments, is also published elsewhere in this issue of the Federal Register.

Under section 505 of the act (21 U.S.C. 355), "new drugs," such as radiopharmaceuticals, must be the subjects of approved new drug applications (NDA's) or abbreviated new drug applications (ANDA's) before

marketing. In order to be approved, the products must be shown to be safe and effective for their intended uses through adequate and well-controlled studies (21 Ú.S.C. 355(d)). Investigational use of drug products is governed, in general, by the requirements in part 312 (21 CFR part 312). Special provisions concerning radioactive drugs for certain research uses are contained in FDA regulations at 21 CFR 361.1. Under these special provisions, use of radioactive drug products in human subjects during the course of limited kinds of research projects may occur if the use is approved by a properly constituted Radioactive Drug Research Committee and if other conditions are met.

Section 502 of the act (21 U.S.C. 352) sets forth misbranding provisions applicable to drug products. Among other circumstances, a drug is considered misbranded if the product labeling is false or misleading or if the drug is dangerous to health when used as suggested in the labeling (21 U.S.C. 352(a) and (j)). For prescription drugs, section 502(n) of the act describes certain information that must be included in all advertisements or other printed materials. FDA's regulations also establish labeling and advertising requirements in more detail (21 CFR parts 201 and 202).

Section 510 of the act (21 U.S.C. 360) requires persons who own or operate establishments for the manufacture, preparation, propagation, compounding, or processing of drugs (with certain exceptions) to register the establishments with FDA. Individuals who must register their establishments under section 510 of the act must also file a list of all the drugs being made or processed at the establishment. Drug registration and listing regulations are codified at part 207 (21 CFR part 207).

II. Guidance: Regulation of PET Radiopharmaceuticals

FDA regulates PET radiopharmaceutical drug products used in purely physiologic research, where the results of such research are not used to guide patient management or treatment decisions, as well as in investigational clinical trials and clinical practice. All facilities that manufacture PET radiopharmaceuticals must be registered with FDA in accordance with FDA regulations on the registration and listing of producers of drugs (part 207). Facilities that manufacture PET radiopharmaceuticals are not exempt from registration under §1A207.10 because their activities do not fall within the scope of the regular course of the practice of the profession of pharmacy. This policy statement