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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, FOOD AND DRUG ADMINISTRATION

NUCLEAR PHARMACY GUIDELINE

CRITERIA FOR DETERMINING WHEN TO REGISTER AS A DRUG ESTABLISHMENT

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NUCLEAR PHARMACY GUIDELINE
CRITERIA FOR DETERMINING WHEN TO REGISTER AS A
DRUG ESTABLISHMENT

This guideline prepared by the Food and Drug Administration's Center for Drugs and Biologics states the criteria for determining when a nuclear pharmacy is required to register as a drug establishment

REGULATORY HISTORY

In the FEDERAL REGISTER of July 25, 1975 (40 FR 31298), the Food and Drug Administration (FDA) published regulations which terminated a then-existing exemption for radioactive drugs from the investigational new drug requirements of the Federal Food, Drug, and Cosmetic Act (the act). The exemption was originally published in the FEDERAL REGISTER of January 8, 1963 (28 FR 183). The effect of the termination was to require manufacturers and distributors of radioactive drug products to comply with the act and applicable regulations, including requirements for registration, drug listing, current good manufacturing practice, new drug applications, investigational new drugs, labeling, and advertising. With the publication of the termination, the FDA replaced the Nuclear Regulatory Commission (NRC) as the agency responsible for regulating the safety and effectiveness of radioactive drugs as they affect patients. Certain residual authority to control the use of radioactive materials, discussed in greater detail below, remained with the NRC.

The FDA has legislative authority under the Federal Food, Drug, and Cosmetic Act to regulate drugs for human use. Section 510 of the act (21 U.S.C. 360) requires drug establishments to register with FDA. Other provisions of the act provide the authority for FDA to regulate the manufacture, sale, and distribution in interstate commerce of new drugs, to assure that they are safe and effective for their intended use (Secs. 501, 502, 505 of the act; 21 U.S.C. 351, 352, 355). Section 201(p) of the act defines the term "new drug" generally to mean a drug not generally recognized by qualified experts to be safe and effective. It has been the agency's position that all radioactive drugs, including radioactive biological products, are new drugs except for those generally recognized as safe and effective when administered for research under the conditions set forth in § 361.1(b) of the act (21 CFR 361.1(b)).

Under section 510(g)(1) of the act, a pharmacy, including a nuclear pharmacy, is exempt from complying with the need to register as a drug establishment if (1) it operates in conformance with any applicable local laws regulating the practice of pharmacy and medicine, (2) it is regularly engaged in dispensing prescription drugs upon the prescription of practitioners licensed to administer prescription drugs to patients under their care in the course of their professional practice, and (3) it does not manufacture, propagate, compound, or process drugs or devices for sale other than in the regular course of their business of dispensing or selling at retail. Thus, to the extent these requirements are met, a nuclear pharmacy may prepare a radioactive drug without being required to register with FDA.

as a drug establishment under section 510. Under other circumstances, however, registration of a nuclear pharmacy will be required.

As a matter of practice, in addition to nuclear pharmacies, nuclear medicine laboratories under the control of a physician may also prepare radioactive drugs. Section 510(g)(2) of the act specifically permits licensed practitioners to manufacture drugs without having to register as drug manufacturers provided the drugs are solely for use in the course of the practitioner's professional practice.

Because the NRC has legislative authority to license and regulate all aspects of the possession and use of radioactive by-product (i.e., reactor-produced) materials in order to protect health and minimize danger to life or property, it also has certain regulatory authority over radioactive drugs. Both radioactive drug manufacturers and nuclear pharmacies are required, therefore, to comply with applicable regulations of the NRC as well as those of FDA.

In a separate notice also published in the FEDERAL REGISTER of July 25, 1975 (40 FR 31314), FDA announced its intention to clarify the responsibilities of nuclear pharmacies under the act. The notice contained an interim enforcement policy pertaining to nuclear pharmacies. It stated that FDA would not take regulatory action against a nuclear pharmacy that did not comply with the requirements of the act, except when regulatory action was necessary to protect the public health, provided the pharmacy (1) complied with applicable local laws regulating the practice of pharmacy, and (2) was licensed, when applicable, by the NRC or an Agreement

State to possess, use, or transfer radioactive drugs. (An Agreement State is one that, under formal agreement with the NRC, is authorized to license, under Federal law, persons engaged in the possession, use, or transfer of source, by-product or special nuclear materials in that State). FDA adopted this interim enforcement policy in 1975 to avoid any disruption in the practice of nuclear pharmacy and nuclear medicine throughout the United States. FDA concluded that, although radioactive drug manufacturers would be subject to the act, it would not take regulatory action for the failure of nuclear pharmacies to comply with the requirements of the act, under the conditions specified, until the status of nuclear pharmacies was further clarified.

DEVELOPMENT OF NUCLEAR PHARMACIES

Since 1946, when artificially produced radioisotopes became available in quantity, there has been a rapid growth in the medical use of radioactive drugs, including radioactive biological products, to diagnose and treat disease. Radioactive drugs are administered for two different purposes: as a radiation source, and as a radioactive tracer. As a radiation source their principal role is in therapy; as a radioactive tracer they are used primarily for diagnostic purposes.

When radioactive drugs first became generally available, they were usually prepared by commercial drug manufacturers under approved new drug applications (NDA's) and shipped to users in a form suitable for direct

administration to patients. As the use of radioactive drugs increased within hospitals, units within hospitals were often created to receive and store all incoming radioactive drugs. In most hospitals—where, in fact, most radioactive drugs are administered—those units often became part of the pharmacy department. Pharmacies employing registered pharmacists and other personnel having specialized training and experience in compounding, preparing, storing, and dispensing radioactive drugs became known specifically as "nuclear pharmacies."

Initially, the activities of a nuclear pharmacy included (1) purchasing a commercially prepared radioactive drug from a drug manufacturer who held an approved NDA and dispensing the drug in its original unopened container, (2) dispensing a single dose from a multiple-dose container of a commercially prepared radioactive drug, and (3) diluting (including adjustments of buffers, bacteriostatic agents, and stabilizers) and repackaging a commercially prepared radioactive drug for subsequent use or distribution. As the training and experience of nuclear pharmacists increased, some nuclear pharmacies began preparing their own radioactive drugs.

One method used by nuclear pharmacies to prepare radioactive drugs was to add a radionuclide to a nonradioactive substance, usually a drug product, resulting in what is referred to as a "labeled compound." In nuclear medicine the term "labeling" refers to the process of adding a radioisotope to a suitable nonradioactive substance. In this document, this process is referred to as "radiolabeling" to avoid confusion with the term "labeling" as defined in section 201(m) of the act.

As technology developed, and in order to reduce the radiation dose to patients, radioactive drugs with shorter-lived radionuclides were introduced. Because of their short half-lives, many of these drugs must be prepared in a final dosage form shortly before they are to be administered to patients. Thus, these drugs had to be prepared at a facility close to where they would be administered. Otherwise the delivery time could be so long that significant radioactive decay would take place before the drug was administered. The ability to prepare radioactive drugs with short half-lives became possible, in part, through the use of a radionuclide generator. A radionuclide generator contains a glass or plastic column filled with an adsorbant, such as a resin or alumina, in which the long-lived "parent" radionuclide is retained. Radioactive decay of the long-lived parent radionuclide results in the production of a short-lived "daughter" radionuclide which is eluted by passing an appropriate liquid or gas through the column. These radionuclides are then used by a nuclear pharmacy to prepare short-lived radioactive drugs, often by using a nonradioactive kit. A "nonradioactive kit" or "reagent kit" contains all the necessary ingredients, except the radionuclide, for making a radioactive drug product. By adding the radionuclide to the nonradioactive kit according to the directions accompanying the kit, a radioactive drug product of specified purity can be produced, often just prior to administration. Most nonradioactive kits are prepared by a commercial manufacturer under an approved NDA, but some nuclear pharmacies are now preparing their own kits.

Another aspect in the development of nuclear pharmacies has been their physical location and extent of activities. Most nuclear pharmacies are located in hospitals and dispense radioactive drugs only within the institution in which they are located. As the practice of nuclear pharmacies has matured, some nuclear pharmacies, although located in a particular institution, may supply radioactive drugs to other institutions that do not have nuclear pharmacies. In other instances, some nuclear pharmacies may be completely independent of any institution and may supply radioactive drugs to a number of institutions and practitioners. Distribution of radioactive drugs by a nuclear pharmacy may thus be limited to (1) one institution, (2) a few institutions and practitioners in the vicinity of the nuclear pharmacy, or (3) a large number of institutions and practitioners in a large metropolitan or geographic area, which may be located in more than one State.

ACTIVITIES OF NUCLEAR PHARMACIES

Activities of a nuclear pharmacy may include:

- o Purchasing a commercially prepared radioactive drug product which is marketed under an approved NDA and dispensing the drug in its original unopened container.

- o Repacking a radioactive drug product which is the subject of an approved NDA for subsequent use or distribution.

- o Dispensing a single dose, or series of single doses, from a multiple-dose container of an approved radioactive drug product. For example, dispensing single capsules of radioactive sodium iodide, drawing a single dose of a radioactive drug into a syringe, or drawing a number of single doses of a radioactive drug into syringes.

- o Diluting and repackaging an approved radioactive drug product, such as adding water for injection to reduce the concentration of the active components, and adjustment of buffers, bacteriostatic agents and stabilizers.

- o Eluting an approved radionuclide generator and using the eluate to radiolabel a nonradioactive kit to prepare a radioactive drug product.

- o Manufacturing a nonradioactive kit for subsequent use in preparing a radioactive drug product.

- o Preparing a radioactive drug product by using a commercially prepared radionuclide or a radionuclide obtained from a nuclear reactor or particle accelerator to which the nuclear pharmacy has access.

Some activities of a nuclear pharmacy clearly involve pharmacy practice that qualify for the statutory exemption available to pharmacies. Other activities, however, are operations that would require the establishment to

register under section 510 of the act. Nuclear pharmacies that are required to register under the act will also be subject to the drug listing provisions of section 510 of the act and FDA's regulations under 21 Part 207, the current good manufacturing practice requirements of section 501 of the act and FDA's regulations under 21 CFR Parts 210 and 211, and the factory inspection provisions of section 704 of the act. A nuclear pharmacy, particularly one that is required to register, may also be subject to the new drug provisions of section 505 of the act and FDA's regulations under 21 CFR Parts 310, 312, and 314.

All pharmacies, including nuclear pharmacies that qualify for the statutory exemption, are subject to section 501 of the act. Section 501(a)(2)(B) of the act deems a drug to be adulterated if the facilities or controls used for its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practices. Although nuclear pharmacies are required to comply with section 501(a)(2)(B) of the act, it has not been the policy of FDA to apply the current good manufacturing practice regulations under 21 CFR Parts 210 and 211 to pharmacies as these regulations are not specifically applicable to many pharmacy operations.

All pharmacies, including nuclear pharmacies, are also subject to the factory inspection provisions of section 704 of the act. This section authorizes, among other things, the inspection of any factory, warehouse, or establishment in which food, drugs, devices, or cosmetics are manufactured, processed, packed, or held for introduction into interstate

commerce or after such introduction into interstate commerce. Thus, as establishments holding drugs after their introduction into interstate commerce, all pharmacies, including nuclear pharmacies, are subject to inspection under this provision. In addition, nuclear pharmacies that are required to register as drug establishments under section 510 of the act are subject to more extensive provisions of the inspectional authority of section 704. Although subject to inspection, the agency is not required to inspect, and except for reasonable cause normally does not inspect pharmacies, including nuclear pharmacies, operating entirely under the pharmacy exemptions in the act. However, the agency will be required, under section 510(b) of the act (21 U.S.C. 360(b)), to inspect pharmacies, including nuclear pharmacies, that are registered as drug establishments under section § 510(b) of the act.

DEVELOPMENT OF GUIDELINE

To better understand the nature of the practice of nuclear pharmacy, including the types of activities and organizational settings in which these activities are performed, FDA has met with a number of professionals, professional organizations, and Federal and State agencies having an interest in nuclear medicine and pharmacy. A meeting, jointly sponsored by the State of Washington Radiation Control Unit and FDA's regional office in Seattle, was held in Seattle on November 12 and 13, 1975. Representatives of a number of State radiation control agencies,

two State boards of pharmacy, the American Pharmaceutical Association, and several practicing nuclear pharmacists and others attended this meeting. Issues discussed at this meeting were: (1) What is a nuclear pharmacist, and what kind of qualifications should he/she have for preparing and dispensing radioactive drugs? (2) What credentialing requirements are appropriate for nonpharmacist dispensers of radioactive drugs? (3) What is the definition of radiopharmacy or nuclear pharmacy, and what constitutes a prescription for a radioactive drug? (4) What are the requirements for the preparation and supply of radioactive new drugs including those for investigational purposes? A summary of this meeting is available for inspection at FDA's Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD, 20857, under Docket No. 80D-0069.

FDA believes the first three questions involve primarily State and local laws regulating the practice of pharmacy. However, under the act the answers to these questions may determine, in a given situation, whether a pharmacy is exempt from the registration provisions of the act. Thus the licensure procedures that designate a person as being a pharmacist, the extent that a pharmacist may delegate authority, and the type of order that qualifies as a prescription are all matters that are determined under State laws, but they may also affect the application of the act to pharmacies.

To aid the agency in establishing criteria to determine what activities of a nuclear pharmacy require registration, a subcommittee of FDA's Radiopharmaceuticals Advisory Committee was appointed in October

1975 to consider and report on issues relating to nuclear pharmacy. Specifically, the subcommittee was requested to consider the following two questions: What types of operations engaged in by nuclear pharmacies should be regulated to some degree by FDA? What is the relative urgency for issuing new regulations or statements of policy, if they are needed?

The subcommittee reported to the Radiopharmaceuticals Advisory Committee on April 15, 1976. In preparing its report the subcommittee received suggestions and recommendations from numerous individuals and organizations. In addition, it considered the public testimony presented on these two questions before the full committee in April 1975, and the statements and discussions at a meeting of the subcommittee in January 1976. A copy of this report is also available for inspection at FDA's Dockets Management Branch (address above) under Docket No. 80D-0069.

In considering which nuclear pharmacy operations should be regulated by FDA, the subcommittee concluded that if the radioactive drug was prepared and dispensed under a prescription, the laws and regulations governing the practice of pharmacy and medicine at the State level should apply and the nuclear pharmacy should be considered as engaging in the practice of pharmacy. On the other hand, the subcommittee stated that the presence of a third party in the distribution of a prescription drug, between the location where the product is formulated, compounded, or manufactured and the point where it is administered to patients, changes the practice to one of manufacturing. Examples of this type of situation that were cited by the subcommittee included one in which a nuclear

pharmacy sells radioactive drugs to a second pharmacy for dispensing by the second pharmacy under a prescription, and one in which a nuclear pharmacy sells to other pharmacies bulk quantities of nonradioactive kits that it develops. In each case the first pharmacy would be a manufacturer under the act and be required to register under Section 510 of the act.

The subcommittee also recognized that radioactive drugs are often administered by a nuclear medicine unit in a single institution. Such a nuclear medicine unit may operate a nuclear pharmacy and maintain control over any radioactive drug manufactured or compounded within the pharmacy until it is dispensed. Here, the subcommittee concluded that the high level of control exercised over the drug precluded any need for registration.

The subcommittee recommended to FDA that substantive changes in FDA regulations, as they pertain to true nuclear pharmacies, were not needed. The subcommittee recommended that individual State boards of pharmacy rather than FDA should regulate nuclear pharmacies in the same manner as they now regulate traditional pharmacies which do not compound or dispense radioactive drugs.

At the same time, the subcommittee recommended that FDA clarify "the issue of nuclear pharmacy manufacturing versus traditional pharmacy compounding with a policy statement; this statement should indicate that the same criteria will be used in making this determination for radioactive drugs as those which are used for nonradioactive drugs. This statement will also affirm that certain of the operational procedures in which some nuclear pharmacies engage are, in fact, manufacturing, and must be regulated as such."

CRITERIA FOR DETERMINING WHEN A NUCLEAR PHARMACY

MUST REGISTER AS A DRUG ESTABLISHMENT

FDA agrees with the subcommittee's recommendation that, to the extent practicable, the criteria for registration as a drug establishment for nuclear pharmacies should be the same as those for traditional pharmacies. The agency further agrees with the subcommittee that regulations applicable to nuclear pharmacies contemplated in the July 25, 1975 notice are not needed at this time and that FDA can fulfill its regulatory responsibilities in this area by issuing a guideline on the subject. This guideline also responds to the subcommittee recommendation that FDA notify State boards of pharmacy and other State and Federal agencies of FDA's policy in the area of nuclear pharmacies.

Section 510(g)(1) of the act (21 U.S.C. 360(g)(1)) states that pharmacies which maintain establishments in conformance with any applicable local laws regulating the practice of pharmacy and medicine are exempt from the drug registration provisions of the act. For the exemption to apply they must be regularly engaged in dispensing prescription drugs or devices, upon prescriptions of practitioners licensed to administer such drugs or devices to patients under the care of such practitioners in the course of their professional practice, and they must not manufacture, prepare, propagate, compound, or process drugs or devices for sale other than in the regular course of their business of dispensing or selling drugs or devices at retail. Because many States do

not appear to have laws that apply specifically to the practice of nuclear pharmacy, and may not have mechanisms specifically designed for certifying nuclear pharmacists, and because many nuclear pharmacies require specially trained personnel whose activities resemble those of drug manufacturers more than those of traditional pharmacy practice, FDA does not believe that the "pharmacy" exemption of the drug registration provisions of section 510(g)(1) of the act (21 U.S.C. 360(g)(1)) applies to all so-called "nuclear pharmacies." FDA's regulation of nuclear pharmacies will be based on a reasonable application of the provisions of section 510(g)(1) of the act to nuclear pharmacies and it will treat these nuclear pharmacies as other pharmacies have been traditionally treated under this section. Therefore, a pharmacy, including a nuclear pharmacy, whose activities are consistent with section 510(g)(1) of the act will be exempt from registering as a drug establishment and from complying with other requirements that flow from registration. Conversely, a pharmacy, including a nuclear pharmacy, whose activities are outside the provisions of section 510(g)(1) of the act will be subject to the registration provisions of the act and to those requirements that are concomitant to registration.

To operate under applicable local laws regulating the practice of pharmacy and medicine may mean that a nuclear pharmacy must be operated under the supervision of a pharmacist, registered in the State to practice pharmacy. In States with such requirements, nuclear medical laboratories operated by chemists or physicists who are not also registered pharmacists will not qualify for the exemption from registration under section 510(g)(1) of the act regardless of the activity in which the facility engages.

Certain activities of nuclear pharmacies are clearly within the pharmacy exemption of section 510(g)(1) of the act. For example, in a situation where the nuclear pharmacy is operating within applicable local laws regulating the practice of pharmacy and only prepares and dispenses a radioactive drug upon receipt of a "valid prescription," the pharmacy exemption clearly applies. FDA views the term "valid prescription" to mean an order that qualifies as a prescription under State law for a prescription drug, from a practitioner licensed to administer the drug to a patient under the care of the practitioner in the course of his or her professional practice. Further, although the act does not define the term "prescription," section 503(b)(2) of the act states that any drug dispensed by filling a prescription of a practitioner licensed by law to administer the drug is exempt from certain of the misbranding provisions of the act if it bears a label containing the name and address of the dispenser, the serial number and date of the prescription or its filling and, if stated in the prescription, the name of the patient and directions for use and cautionary statements, if any, contained in the prescription. Thus, except for prescriptions for controlled drugs, Federal law requires the name of the patient to appear on the label of the prescribed drug only when this information is stated in the prescription by the physician. However, without stating the precise format of a prescription, the act contemplates that certain information will ordinarily be supplied by the licensed practitioner to the pharmacist. Further, the act implies that a prescription is written with a particular patient in mind. In addition, many States, as part of their pharmacy practice statutes, require the patient's full name.

In the traditional practice of pharmacy, prescriptions are usually handled differently depending upon whether the prescriber and patient are in an institutional setting or in a private setting. In the institutional setting, the patient's prescription is usually forwarded to the pharmacy by the nursing staff and the prescribed drug is then sent back to the nursing staff for storage without the institutionalized patient ever obtaining possession of the prescription or of the prescribed drug. In the private setting, the prescriber usually hands the prescription to the patient, who takes it to their pharmacy of choice and receives the prescribed drug from the pharmacist. In either situation, however, the prescription is normally written for a specific patient. Rarely, in the private setting, is a prescription written for more than one patient. One example of such a situation would be when all members of a single family are being treated for the same condition with the same drug, e.g., pinworms. In such a situation it is considered appropriate to write and dispense one prescription for the entire family rather than write and dispense separate prescriptions for each family member. However, in such a situation, a member of the family normally obtains possession of the prescription and takes it to a pharmacy to be filled.

The agency believes that, although traditional pharmacy practice concepts should apply to nuclear pharmacies to the extent possible, the unique nature involved in the preparation, handling and administration of radioactive drugs might require some departures from the traditional pharmacy practice. For example, when dealing with radioactive drugs the

patient, whether or not in an institution, normally does not obtain possession of the prescription or of the prescribed drug. Usually, the physician orders the drug from a nuclear pharmacy which dispenses it directly to the physician for administration to the patient under the physician's supervision. Further, because most radioactive drugs are intended for diagnostic purposes, they must be administered to the patient at a facility having the specialized equipment necessary for the diagnostic procedure to be performed.

The agency is also aware that in nuclear pharmacy there are instances where physicians in private practice specializing in nuclear medicine, as well as physicians specializing in nuclear medicine connected with a private clinic, will schedule several patients to undergo the same diagnostic procedure using the same injectable radioactive drug on a particular day. Rather than order a separate container of the drug for each patient, a multiple dose container of the radioactive drug to be administered to all the patients undergoing the same procedure is ordered. In addition, the physician or clinic may have a standing order with the nuclear pharmacy to supply a multiple-dose container of a particular radioactive drug on a certain day of the week to be administered to patients scheduled to undergo a common diagnostic procedure. The practice of having one order cover several unrelated, but scheduled patients and supplying a multiple-dose container for such patients is not normally considered to be the traditional pharmacy practice. However, the agency has evaluated this practice with respect to the dispensing of

radiopharmaceuticals and concludes that, while it is a departure from traditional pharmacy practice, it is, given the unique circumstances of nuclear medicine, a reasonable variant of it, and thus appropriately considered accepted pharmacy practice. Accordingly, FDA will not require a nuclear pharmacy engaging in such activities to register as a drug establishment provided the dispensing pharmacy maintains a hard copy of the prescription or physician's order as required by section 503(b)(2) of the act and the pharmacy otherwise complies with all aspects of traditional pharmacy practice. Although the above referenced practices will not subject a nuclear pharmacy to registration with the FDA as a drug establishment, a nuclear pharmacy should also determine that such practices are consistent with applicable State pharmacy laws.

In certain situations, the fact that the preparation of the radioactive drug results in the preparation of a new drug or requires more technical equipment and expertise than that of a nonradioactive prescription drug does not nullify the pharmacy exemption. Likewise, neither the location of the patient nor the location or ownership of the nuclear pharmacy would nullify the pharmacy exemption. Several different situations involving a nuclear pharmacy operating under applicable State pharmacy laws and preparing and dispensing a radioactive drug upon receipt of a valid prescription are set forth in the examples given below.

In other situations, the activities of a nuclear pharmacy will be clearly outside the pharmacy exemption. For example, if a nuclear pharmacy prepares a nonradioactive kit for sale to other nuclear pharmacies which add the radionuclide for dispensing under prescription,

the activity of the first pharmacy clearly falls outside the pharmacy exemption. The examples below give several situations in which the pharmacy exemption does not apply because there is no prescription.

Nonetheless, in some situations, it will not be clear whether the activities of a nuclear pharmacy will fall within the pharmacy exemption. Many involve nuclear pharmacies that are located within a hospital. To determine if the pharmacy exemption applies, FDA believes it will be helpful to compare the activities of a hospital nuclear pharmacy with the activities of a traditional hospital pharmacy. In addition to filling and dispensing valid prescriptions for both inpatients and outpatients, a traditional hospital pharmacy may also send prescription drugs to a ward or clinic within the hospital upon the order of an authorized person. The drug, when sent to the ward or clinic, is not intended for any specific patient, but is intended to be used by the ward or clinic as needed when a licensed practitioner orders the drug in a patient's medical record. The term "ward or floor stock" has been applied to drugs made available in this manner. Because these drugs are under the control of the pharmacy and the institution within which the ward or clinic is located and the drug is prescribed by a licensed practitioner for a particular patient, this activity will be considered to fall within the pharmacy exemption. Under the same rationale, if a hospital nuclear pharmacy prepares a radioactive drug and dispenses it to a nuclear medicine clinic or department located within the hospital upon an order for the drug by an authorized person, even though the drug were

in a multiple-dose container, the pharmacy exemption would apply. Of course, because of their short half-life, it would not be expected that radioactive drugs would be maintained as ward or floor stock in the same manner as other drugs.

On occasion, a traditional hospital pharmacy may, upon request of another pharmacy, send a drug product in its original unopened container to another pharmacy. This situation may arise when the second pharmacy finds that it is out of stock of a particular drug product. Provided the first pharmacy did not manufacture the drug product, it would not be required to register for such an activity. Likewise, a nuclear pharmacy can send a radioactive drug product marketed under an approved NDA in its original unopened container to another nuclear pharmacy upon request without being subject to the registration provision of the act.

The agency is aware that some nuclear pharmacies have been instrumental in the development of new radioactive drugs or new uses for existing radioactive drugs. Nuclear pharmacies may also prepare new radioactive drugs that are not commercially available, but whose use and preparation have been described in the medical literature. Physicians that write a prescription for a drug that must be compounded by a pharmacist bear the professional responsibility to base its use on sound scientific rationale or medical evidence. The agency believes that as long as the pharmacist does not engage in activities that fall outside the normal practice of pharmacy, such use of a drug in the practice of medicine does not require

an Investigational New Drug Application (IND) or NDA. However, if a pharmacist does engage in activities that fall outside the normal practice of pharmacy, the pharmacy would legally have to be registered notwithstanding that it may be filling physician's orders. Therefore, depending upon how such a drug is prepared, promoted, and distributed, its preparation may fall outside the normal practice of pharmacy and not qualify for the pharmacy exemption. In such cases, even if the drug were dispensed on prescription, the nuclear pharmacy would have to comply with the new drug provisions of the act even though it may not be required to register under section 510 of the act (though it may be required to do both). Because the particular circumstances surrounding the operation of the nuclear pharmacy would have to be examined in detail to determine whether the pharmacy is operating within the practice of pharmacy, such situations will have to be decided on a case-by-case basis. An example where a nuclear pharmacy would have to comply with the new drug provisions is where the nuclear pharmacy has developed a rechargeable generator, such as a generator used in preparing Technetium Tc 99^m by being charged with Molybdenum Mo 99. Each recharging of the generator is considered the manufacturing of a new drug by the agency. An NDA would be required to cover all phases in the development and use of this type of generator, from its construction to the finished product, including how many times it could be recharged.

It is obvious from this discussion that certain types of nuclear pharmacy activities may be conducted under the pharmacy exemption while others conducted by the same nuclear pharmacy may not. The nuclear

pharmacy must register with FDA for activities that are not within the pharmacy exemption, irrespective of how small a portion they are of the pharmacy's total activities. Under this policy some nuclear pharmacies not now registered will be required to register. Nonetheless, this guideline does not impose new requirements on these establishments. Rather, it applies existing requirements to facilities whose functions have for the first time been examined and quantified. Pharmacies, including nuclear pharmacies, are considered as drug establishments and are subject to the provisions of the Federal Food, Drug, and Cosmetic Act to the extent they are not specifically exempt, including the provisions of sections 501, 502, 503 and the applicable part of the factory inspection provision in section 704. Establishments that are required to register are also subject to the current good manufacturing practice requirements of section 501 of the act and FDA's regulations under 21 CFR Parts 210 and 211, and the factory inspection provisions of section 704 of the act. In addition, an establishment manufacturing a "new drug", or a pharmacy that has itself developed a new drug, will also be subject to the provisions of section 505 of the act and applicable FDA regulations under 21 CFR Parts 310, 312, and 314. Nuclear pharmacies may obtain information and appropriate forms for registering as a drug establishment from FDA Regional or District Offices or by writing directly to the Center for Drugs and Biologics, Drug Listing Branch (HFN-315), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

The examples that follow cover most activities of nuclear pharmacies. Obviously, they cannot represent all possible situations. In addition, it must be remembered that in many situations the particular circumstances surrounding the operation of a nuclear pharmacy may have to be examined in detail to determine whether the pharmacy is operating within the practice of pharmacy, and such situations will have to be decided on a case-by-case basis. Anyone may seek an opinion whether a particular activity qualifies for the pharmacy exemption by writing to the person responsible for maintaining the guideline named above.

Therefore, the agency makes available the following examples reflecting the agency's policy for examining functions of a nuclear pharmacy to determine if they are required to register.

EXAMPLES OF WHEN A NUCLEAR PHARMACY MUST REGISTER
AS A DRUG ESTABLISHMENT

Source of drug	Activities of the nuclear pharmacy	Registration required
A. Radioactive drug is supplied by a manufacturer. (Product is subject of an approved NDA or IND)	1. Dispenses the drug under a prescription in the manufacturer's original container.	1. No
	2. After storing the drug, ships the drug in the manufacturer's original container to another nuclear pharmacy or to a physician with or without having received a prescription.	2. No

3. Fills the drug into single or multiple-dose containers in anticipation of a future need and its subsequent dispensing under a prescription. 3. No

4. Dispenses a drug that was diluted or filled into single or multiple dose containers upon receipt of a prescription. 4. No

5. Dilutes or fills the drug into single- or multiple-dose containers and dispenses the drug without a prescription but upon receipt of an appropriate order, for use within the same institution. 5. No

6. Upon an order from a physician, dilutes or fills the drug into multiple-dose containers and ships the drug to the physician as part of accepted pharmacy practice. 6. No

7. Dilutes or fills the drug into single- or multiple-dose containers and ships it without a prescription to another nuclear pharmacy or institution that, irrespective of its location or ownership, is recognized as a separate entity by FDA. 7. Yes

B. Radioactive drug (not involving use of a nonradioactive kit) prepared by the nuclear pharmacy.

1. Upon receipt of a prescription, prepares a radioactive drug and dispenses it. 1. No

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| 2. Prepares a radioactive drug in anticipation of a future need and its subsequent dispensing under a prescription. | 2. No |
| 3. Prepares a radioactive drug and dispenses it without a prescription, but upon receipt of an appropriate order for use within the same institution. | 3. No |
| 4. Operates an accelerator or nuclear reactor to produce radionuclides and radiochemicals to manufacture radioactive drugs to be dispensed under a prescription. | 4. No |
| 5. Upon a request from a physician, prepares a drug in multiple-dose containers and ships the drug to the physician as part of accepted pharmacy practice. | 5. No |
| 6. Prepares a radioactive drug and ships it without a prescription to another pharmacy or institution that, irrespective of its location or ownership, is recognized as a separate entity by FDA. | 6. Yes |
| 7. Prepares radiochemicals and ships them to other nuclear pharmacies or institutions as drug components. | 7. Yes |
| C. A reagent kit and generator are supplied by a manufacturer. (The kit and generator are subject to an approved NDA or IND). | 1. Radiolabels the reagent kit according to the manufacturer's directions and dispenses the drug under a prescription.
1. No |

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|---|---|--------|
| | 2. Radiolabels a reagent kit in anticipation of a future need and its subsequent dispensing under a prescription. | 3. No |
| | 3. Upon request from a physician, radiolabels a reagent kit and ships the drug to the physician as part of accepted pharmacy practice. | 3. No |
| | 4. Radiolabels a reagent kit and ships it without a prescription to another pharmacy or institution that, irrespective of its location or ownership, is recognized as a separate entity by FDA. | 4. Yes |
| D. A reagent kit is prepared by the nuclear pharmacy. | 1. Upon receipt of a prescription, prepares and radiolabels the reagent kit and dispenses it. | 1. No |
| | 2. Prepares a reagent kit in anticipation of a future need. Upon receipt of a prescription, radiolabels and dispenses it. | 2. No |
| | 3. Upon a request from a physician, prepares reagent kits and ships them (either before or after radiolabeling) to the physician as part of accepted pharmacy practice. | 3. No |
| | 4. Prepares a reagent kit and ships it without a prescription, either before or after radiolabeling, to another pharmacy or institution that, irrespective of its location or ownership, is recognized as a separate entity by FDA. | 4. Yes |

E. Radioactive drug or reagent kit obtained from another nuclear pharmacy, institution, or practitioner.

1. Uses the radioactive drug or reagent kit to perform one or more steps in the manufacture of a radioactive drug as a service for the nuclear pharmacy or institution that supplied the radioactive drug or kit, i.e., custom manufacturing.

1. Yes

Attachment: Summary of Comments on Proposed Guideline for Nuclear Pharmacies Describing Activities that Require Registration as a Drug Establishment and Agency Responses.

SUMMARY OF COMMENTS ON PROPOSED GUIDELINE FOR NUCLEAR PHARMACIES
DESCRIBING ACTIVITIES THAT REQUIRE REGISTRATION AS A DRUG ESTABLISHMENT
AND AGENCY RESPONSES

[Docket No. 80D-0069, 75N-0069]

In the FEDERAL REGISTER of April 11, 1980, (45 FR 24920) the agency announced the availability of a proposed guideline that would assist nuclear pharmacies in determining if they are required to register as drug establishments under section 510 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360). Twelve comments were received in response to the proposed guideline. A summary of the comments and the agency's response to each are as follows:

1. Several comments cited specific fact situations and asked if registration was necessary. The specific questions were as follows:

(a) One comment asked if registration is necessary if a nuclear pharmacist purchases raw materials, prepares a radioactive drug product and then dispenses the drug product upon receipt of a prescription.

(b) One comment asked if registration is required if a nuclear pharmacist prepares a radioactive drug in bulk at one location, transfers the bulk drug to a second pharmacy where the same nuclear pharmacist also works and uses the material in filling a prescription.

(c) Several comments asked if registration is required if a pharmacist prepares a prescription using a commercial reagent kit, but deviates from the instructions accompanying the reagent kit, such as by adding ascorbic acid.

(d) One comment asked if registration is required when a technician prepares radioactive drugs under either direct or indirect supervision of a physician and then delivers the drug to the physician at multiple sites.

Certain activities of nuclear pharmacies are clearly within the pharmacy exemption of section 510(g)(1) of the Act (21 U.S.C. 360(g)(1)). Likewise, certain other activities of nuclear pharmacies will be clearly outside the pharmacy exemption. However, in many situations, the particular circumstances surrounding the operation of a nuclear pharmacy may have to be examined in detail to determine whether the pharmacy is operating within the practice of pharmacy and such situations will have to be decided on a case-by-case basis. Therefore, the following responses to the question posed by the comments are generalized and are not intended to resolve individual fact situations. Persons seeking guidance on individual situations should contact Division of Drug Labeling Compliance (HFN-310), Office of Compliance, Center for Drugs and Biologics, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, (301)443-7281.

(a) Normally, a nuclear pharmacy that prepares a drug product from raw materials and dispenses it under a prescription is not required to register. (See B. 1. of the guideline).

(b) The fact that the same nuclear pharmacist is involved with the drug at two pharmacies is not relevant to the need to register, nor is necessarily the fact that both pharmacies have common ownership. The agency would have to examine such an arrangement as a whole. However, FDA would consider one relevant factor to be whether the local State Board of Pharmacy recognized the two pharmacies as a single entity and issued them

a single license. In such a case transfer would likely not require registration. However, if a state board considered the pharmacies as two distinct entities, and required separate licensure, then the pharmacy that planned to ship the bulk material would likely be required to register as a drug establishment. Because state pharmacy boards may differ on their treatment of such arrangements, other factors would normally also be considered.

(c) The guideline did not discuss modifications that might be made to an approved reagent kit because issues apart from registration are primarily involved. The agency reviews considerable data before approving an NDA for a reagent kit and concludes that if the manufacturer's instructions are followed, a safe and effective radioactive drug will be produced from the reagent kit. Thus, if the instructions are followed, a physician can be assured that the product prescribed has the properties it purports to possess. If a pharmacist deviates from the manufacturer's instruction, apart from as a prescriber may have directed, the possibility of misbranding or adulterating the drug product must be considered. The addition of ascorbic acid as cited here or other uses of a pharmaceutical necessity in compounding a prescription does not subject the pharmacy to registration, but pharmacists are not exempt from the misbranding and adulteration provisions of the act and must rely to a large degree on their professional judgment as to when and the extent to which modifications to an approved new drug are appropriate.

(d) Registration would not be required if a technician prepares radioactive drugs under the supervision of a physician solely for use by

that physician in the course of his or her professional practice.

However, registration would be required if the drugs are used by other physicians, or if the drugs are sold to the multiple sites mentioned in the comment.

2. Several comments asked if practices such as modifying a reagent kit would make the resulting product a new drug.

If the nuclear pharmacist modifies a kit as directed by prescription, and dispenses it under the prescription, an NDA would not normally be needed. (See, however, the response to comment 3 for factors to be considered). If distributed without a prescription, however, the NDA requirements would apply. Whenever an NDA is not required, however, the pharmacy must keep in mind the adulteration and misbranding concerns expressed in the response to 1.(c) above.

3. Some comments requested the agency to give examples of specific situations in which a new drug application (NDA) or exemption for investigational use of a new drug (IND) would be required. One comment stated it was not conceivable that an NDA or IND would ever be required if an order from a physician for a radioactive drug is dispensed by a nuclear pharmacy for the physician's own use (examples B7 and D4 of the draft guideline) or in response to a prescription order of a physician.

Although the primary intent of this guideline is to describe activities of nuclear pharmacies that require registration as drug establishments, the draft guideline did indicate that in some situations an IND or NDA may be required. These situations would be unusual and for this reason, the parenthetical statements that an IND or NDA may be required included in the draft have been omitted from the examples of

when a nuclear pharmacy must register as a drug establishment. Such situations, nevertheless, could occur. As stated in the text portion of the guideline, concerning the development of new radioactive drugs or new uses of a radioactive drug, ". . . depending upon how such a drug is prepared, promoted, and distributed, its preparation may fall outside the normal practice of pharmacy and not qualify for the pharmacy exemption. In such cases, even if the drug were dispensed on prescription, the nuclear pharmacy would have to comply, with respect to the products it produced, with the new drug provisions of the act, even though it may not be required to register under section 510 of the act." Such circumstances are commonly found when an individual physician is the sponsor of an IND for a radiopharmaceutical. Thus, application of the new drug provisions requires evidence that the pharmacy is performing activities not normally associated with the normal practice of pharmacy and is operating in a manner that subjects it to the new drug provisions of section 505 of the act.

4. One comment was uncertain of the provisions of section 704 of the act and asked about its application to the nuclear pharmacist.

Section 704 of the act authorizes, among other things, the inspection of any factory, warehouse, or establishment in which food, drugs, devices, or cosmetics are manufactured, processed, packed, or held for introduction into interstate commerce or after such introduction into interstate commerce. Thus, as establishments holding drugs after their introduction into interstate commerce, all pharmacies, including nuclear pharmacies, are subject to inspection under this provision. In addition, nuclear pharmacies that are required to register as drug establishments under section 510 of the act are subject to more extensive provisions of

the inspectional authority of section 704. Although subject to inspection, the agency is not required to inspect, and except for reasonable cause normally does not inspect pharmacies, including nuclear pharmacies, operating entirely under the pharmacy exemptions in the act. However, the agency will be required, under section 510(b) of the Act (21 U.S.C. 360(b)), to inspect pharmacies, including nuclear pharmacies, that are registered as drug establishments under this section. The revocation of the interim enforcement policy, published in the FEDERAL REGISTER concurrently with the issuance of this guideline, will mean that nuclear pharmacies qualifying for the pharmacy exemptions will be regulated in the same manner as pharmacies generally and that nuclear pharmacies required to register under section 510 will be regulated like drug manufacturers. The guideline has been expanded (see page 9) to clarify the agency's inspectional authority under section 704 of the act.

5. One comment recommended that the agency develop good manufacturing practice regulations specific to nuclear pharmacies.

The agency does not believe that current good manufacturing practice (GMP) regulations specific for nuclear pharmacies subject to regulation as drug establishments are necessary at this time. The GMP regulations (21 CFR Part 211) provide sufficient detail for drug manufacturers generally and are reasonably applicable to nuclear pharmacies registered as drug establishments. Although some requirements in the regulations are not specific to all types of manufacturing, the agency believes that nuclear pharmacies will be able to initiate additional good manufacturing practices to insure their products meet appropriate standards. With the revocation of the interim enforcement policy and the issuance of these

guidelines, it is expected that many more nuclear pharmacies will register and be inspected by the agency. If these inspections reveal a problem the agency will take appropriate action, including providing further guidance through additional guidelines or proposing additional regulatory requirements. In the meantime, nuclear pharmacists should, on the basis of their professional training and experience as well as their knowledge of the principles of drug manufacturing, be able to apply reasonable control procedures to insure the integrity of their products.

The agency notes that at the 1980 American Pharmaceutical Association's (APhA) Annual Meeting, the APhA House of Delegates adopted two policy statements regarding nuclear pharmacy. These were:

"The American Pharmaceutical Association supports the concept of state boards of pharmacy retaining their authority to regulate all aspects of professional pharmacy practice including nuclear pharmacy practice," and

"The American Pharmaceutical Association urges state boards of pharmacy to promptly adopt appropriate rules and regulations for the practice of nuclear pharmacy using the National Association of Boards of Pharmacy Model Regulations for the Licensure of Nuclear Pharmacies as a model".

The FDA supports these policy statements and encourages States to take appropriate action. Implementation of these policies along with appropriate action by nuclear pharmacy organizations may obviate the need for the agency to develop any additional regulations specific for radioactive drugs.

6. One comment recommended that all nuclear pharmacies be required to perform stability and compatability studies on their containers.

A nuclear pharmacy that performs activities that cause it to be a drug establishment is required to follow the CGMP regulations. These regulations include requirements for containers and closures (21 CFR 211.94) and requirements for stability (21 CFR 211.166). Although these requirements do not apply to nuclear pharmacy operations that fall within the pharmacy exemption, it is still necessary that a nuclear pharmacy, like any other pharmacy, observe standards for containers that assure the stability of the final product.

7. One comment stated that nuclear pharmacists who make their own cold kits should be required to register and suggested that FDA require nuclear pharmacies to manufacture final products from FDA approved kits and prohibit pharmacies from compounding from basic ingredients because stability of radioactive drugs is of utmost importance.

The agency advises that as part of the practice of pharmacy, pharmacists have traditionally been considered free to make use of commercially available materials to practice their profession of compounding and dispensing prescription drug products. Nuclear pharmacists that operate within the pharmacy exemption have this same freedom. However, nuclear pharmacies that routinely prepare a particular type of reagent kit and ship it without a prescription are no longer acting as pharmacies and would be required to register. As noted in the response to comment 6, nuclear pharmacists, as well as other pharmacists, are responsible for assuring that drug products prepared under a prescription meet all standards for that product including proper stability requirements as dispensed.

8. One comment referred to a 1978 opinion handed down by the Attorney General of California, which stated that a pharmacist may compound and dispense an individual prescription for an individual's needs if the components have not been banned even though the product might be a new drug if not dispensed under a prescription. The opinion was that the pharmacist is not creating a market for a new drug but rather acting on the decision of a physician who has exercised independent judgement as to the safety and effectiveness of a particular drug in the treatment of a patient. The comment stated that the proposed guideline indicated that in certain circumstances a nuclear pharmacy may be required to sponsor an IND for a product even though it is dispensed under a prescription. The comment indicated that there may be a conflict between the Attorney General's opinion and the guideline and requested clarification.

The agency does not believe there is any conflict between the California opinion and the guideline. The agency recognizes that medical practice dictates that physicians remain free to use drugs according to their best knowledge and judgement. This may include the request for a drug product to be prepared under a prescription that would be a new drug if prepared by a drug establishment without a prescription. Physicians that write a prescription for a drug that must be compounded by a pharmacist bear the professional responsibility to base its use on sound scientific rationale or medical evidence. The agency agrees that as long as the pharmacist does not engage in activities that fall outside the normal practice of pharmacy, such use of a drug in the practice of medicine does not require an IND or

IDA. However, if a pharmacist does engage in activities outside the normal practice of pharmacy, the pharmacy would legally have to be registered notwithstanding that it may be filling physician's orders. The guideline has been modified in order to clarify this point (see page 21).

9. One comment stated that the example in the last sentence on page 20 of the draft guideline stated that a multi-dose vial filled by a nuclear pharmacist to be administered to several unknown patients may not be recognized as a prescription, but also stated on page 29 that a physician's order for a bulk drug for use in the physician's own practice is not cause for registration. The comment stated that this appeared to be a conflict.

The agency has reevaluated these two examples and has concluded that the need for registration under circumstances involving supplying multiple dose containers of a radioactive drug intended for administration to several patients needs clarification. Because of their short half-life, most radioactive drugs must be administered very promptly. Thus, the example of having a physician order a pharmacist to prepare a radioactive drug in bulk for the physician to store in the office as "office stock" for use, in the physician's practice on appropriate patients as they are seen by the physician was not a realistic example. Therefore, it has been deleted from the guideline. The agency agrees, however, that such an activity, when

performed by a nuclear or traditional pharmacy, should require registration. The guideline has also been modified (see pages 16-19) to clarify that since prescriptions represent a professional relationship between the prescriber, pharmacist and patient, an order written for a multi-dose vial intended for administration to several patients is considered to be a prescription, if the dispensing pharmacy or pharmacist maintains a hard copy of the prescription or physician's order as required by section 503(b)(2) of the act and the pharmacy otherwise complies with all aspects of traditional or accepted pharmacy practice. Although such a practice will not by itself subject a nuclear pharmacy to registration with the FDA as a drug establishment, a nuclear pharmacy should also determine that such practices are consistent with applicable state laws.

10. One comment stated that FDA's belief that a firm should register is not in itself justification to require registration.

FDA's conclusion regarding the registration of certain types of nuclear pharmacies result from a reasoned application of section 510 of the act to the services which those establishments actually provide. The purpose of the guideline is to give guidance to nuclear pharmacies as to when one should register. Some situations regarding the manufacture of radioactive drugs present complex questions. These guidelines are not requirements, but rather an assurance that a person following the guideline will be following procedures acceptable to FDA. Manufacturers are encouraged under FDA guideline procedures to bring to the agency's

attention in advance situations in which a guideline may not be followed. FDA will attempt to resolve in advance disagreements between nuclear pharmacies and FDA over whether registration is required.

11. One comment stated that radiolabeling of a kit, as in example c. 2, is not done according to the directions of a physician. Instead a physician identifies the end product and the pharmacist prepares the prescription for that use.

The agency agrees that a prescription for a radioactive drug does not normally contain instructions for radiolabeling a kit. The intent of this example was to cover those instances where a prescription did contain such information and to distinguish it from example C. 1, which covers those situations where the prescription does not contain information for the labeling of a kit and the nuclear pharmacist prepares the product as set forth in the manufacturer's instructions accompanying the reagent kit. However, since only rarely would a prescription contain instructions for radio labeling a kit, this example has been deleted from the guideline.

12. Several comments stated that the guideline should be integrated with the Nuclear Regulatory Commission (NRC) to limit regulatory concerns to NRC and drug manufacturing concerns to FDA.

As previously stated, the purpose of the guideline is to give guidance to nuclear pharmacies so that they can determine if they should register as drug establishments under section 510 of the Federal Food, Drug, and Cosmetic Act. The determination of whether or not a nuclear

pharmacy should register is entirely within FDA's jurisdiction; there is no overlap with NRC's area of jurisdiction. Therefore, the agency does not see any need to integrate NRC's area of jurisdiction over nuclear pharmacies into the guideline. The agency has, however, supplied a copy of the draft guideline to the NRC for review and comment and will continue to work with NRC to avoid areas of duplication and inconsistencies between the two agency's policies.

13. One comment recommended that the guideline include names of agency personnel to be contacted when nuclear pharmacists have a question concerning their operations.

Agency regulations on guidelines (21 CFR 10.90) require a guideline to contain the name of the person responsible for maintaining the guideline. This person is named as the "contact person" in the notice of availability and this person should be contacted if questions arise as a result of the guideline. If a contact person cannot answer a question he or she will refer the inquirer to FDA employees knowledgeable in the subject matter.

14. One comment stated that a requirement that the patient's name appear on a prescription is inconsistent with contemporary nuclear pharmacy practice because physicians often reassign prescriptions to other patients and is also inconsistent with the guideline examples that physicians may order drug products for their own use. One comment stated that a prescription is defined as an order for a particular patient which would require the patients name to appear on the prescription.

The agency advises that the act (Section 503(b)(2) (21 U.S.C. 353(b)(2)) requires the label of a drug dispensed by prescription to contain the name of a patient when stated in the prescription. Even though the act does not require the patient's name, it does imply that a prescription is written with a particular patient in mind. (See the response to question 9). Further, many states require the patients full name and address on all prescriptions and even when not required by state law, the common accepted practice is for physicians to include the name of the patient on a prescription. The agency recognizes, however, that there are certain differences between traditional pharmacy and nuclear pharmacy. Thus, under the guideline a nuclear pharmacy may prepare a radioactive drug intended for administration to several patients in a multi-dose vial and dispense it provided the dispensing pharmacy engaging in such activities maintains a hard copy of the prescription or physician's order as required by section 503(b)(2) of the Federal Food, Drug, and Cosmetic Act and the pharmacy otherwise complies with all aspects of accepted or traditional pharmacy practice. The guideline contains a more complete discussion of this issue (pages 16-19).

15. One comment objected to the use of the term "diluting" in the guideline. The comment said this gave the impression that pharmacists only "dilute" and dispense when in fact when they dilute a product, they must be concerned with factors such as adjusting buffers, bacteriostatic agents and stabilizers. The word "preparing" was suggested as a substitute.

The agency believes that the use of the term "preparing" in place of "diluting" may be inappropriate because it could imply that the nuclear pharmacist prepared the radioactive drug rather than just performed some activities on a product prepared by a drug manufacturer. However, because "diluting" may also not be appropriate, it has been decided for purposes of this guideline to define the term as including not only simple dilution, but also adjustment of such things as buffers, bacteriostatic agents and stabilizers.