[7590-01]

NUCLEAR REGULATORY COMMISSION

10 CFR PARTS 30 and 35

RIN 3150-AD43

Authorization to Prepare Radiopharmaceutical Reagent Kits and Elute Radiopharmaceutical Generators; Use of Radiopharmaceuticals for Therapy

AGENCY: Nuclear Regulatory Commission.

ACTION: Interim final rule with request for comment.

SUMMARY: The Nuclear Regulatory Commission (NRC) is issuing an interim final rule amending its regulations related to the preparation and the therapeutic uses of radiopharmaceuticals. This interim rule allows licensees who elute generators and prepare reagent kits to depart from the manufacturer's instructions for elution and preparation in the package insert (a part of the Food and Drug Administration (FDA) approved labeling) provided the licensees meet certain conditions and limitations. The interim rule also permits NRC licensees using byproduct material in a radiopharmaceutical for a therapeutic use to depart from the package insert regarding indications and method of administration if certain requirements are met. This amendment is necessary to allow health professionals to provide diagnostic or therapeutic medical results not otherwise attainable or to reduce medical risks to particular patients because of their medical condition while continuing to protect public health and safety adequately. The interim rule applies only to radiopharmaceuticals for which the FDA has approved a "New Drug Application" (NDA).

DATES: Effective date: From [insert date of publication] to [insert date 3 years from the date of publication].

Comment closing date: In view of the interim nature of this rulemaking, comments will be welcome at any time during the three-year period.

ADDRESSES: Submit written comments and suggestions to the Secretary of the Commission, U.S. Nuclear Regulatory Commission, Washington, DC 20555, Attention: Docketing and Service Branch. Hand deliver comments to 11555 Rockville Pike, Rockville, Maryland, between 7:45 a.m. and 4:15 p.m. on Federal workdays.

Copies of the regulatory analysis, environmental assessment, and the comments received on this rule may be examined at the Commission's Public Document Room at 2120 L Street, NW. (Lower Level), Washington, DC. Single copies of the Regulatory Analysis are available from Dr. Anthony Tse, Office of Nuclear Regulatory Research, U.S. Nuclear Regulatory Commission, Washington, DC 20555.

FOR FURTHER INFORMATION CONTACT: Dr. Tse, see ADDRESSES heading, Telephone (301) 492-3797.

SUPPLEMENTARY INFORMATION:

I. Background.

A. Nuclear Medicine.

Radioactive materials are used in drugs in the field of nuclear medicine. Drugs labeled with radioisotopes are known as radiopharmaceuticals. In diagnostic nuclear medicine, patients receive these materials by injection, inhalation, or oral administration. Physicians use radiation detection equipment to visualize the distribution of a radioactive drug within the patient. Using this technology, it is possible to locate tumors, assess organ function, or monitor the effectiveness of a treatment. An estimated 7 million diagnostic nuclear medicine procedures are performed in this country annually. In therapeutic nuclear medicine, radiopharmaceuticals are administered to treat

various medical conditions (e.g., hyperactive thyroid). An estimated 30,000 therapeutic procedures are performed each year.

B. Regulatory Program and Policy Regarding Medical Use of Byproduct Materials.

In a policy statement, "Regulation of the Medical Uses of Radioisotopes," published on February 9, 1979 (44 FR 8242), the NRC stated:

(1) The NRC will continue to regulate the medical uses[1] of radioisotopes as necessary to provide for the radiation safety of workers and the general public.

(2) The NRC will regulate the radiation safety of patients where justified by the risk to patients and where voluntary standards, or compliance with these standards, are inadequate.

(3) The NRC will minimize intrusion into medical judgments affecting patients and into other areas traditionally considered to be a part of the practice of medicine.

The NRC has the authority to regulate medical use to protect the health and safety of patients, but also recognizes that physicians have the primary responsibility for the protection of their patients. NRC regulations are predicated on the assumption that properly trained and adequately informed physicians will make decisions in the best interest of their patients.

Under the Federal Food, Drug, and Cosmetic Act, as amended, the Food and Drug Administration (FDA) regulates drug research and the manufacture and sale

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1 "Medical use," as defined in 10 CFR 35.2, means the "intentional internal or external administration of byproduct material, or the radiation therefrom, to human beings in the practice of medicine in accordance with a license issued by a State or Territory of the United States, the District of Columbia, or the Commonwealth of Puerto Rico." "Medical use" includes the diagnostic and therapeutic use of radiopharmaceuticals in the practice of nuclear medicine, but does not include in vitro diagnostic tests.

of drugs, including radiopharmaceuticals. FDA has regulated the safety and effectiveness of investigational radioactive drugs since 1975, when FDA revoked its 1963 exemption of radioactive drugs from the "Investigational New Drug" (IND) regulation. The NRC withdrew from regulating radioactive drug safety and efficacy to avoid dual Federal regulation, but continues to regulate the radiation safety of workers, patients, and the public.

Each new drug approved for human use by the FDA, including radiopharmaceuticals, has labeling approved by FDA that includes a description of the drug, its pharmacology, indications for use, contraindications, warnings, adverse reactions, dosage and administration, and other information. The labeling of certain drugs, including some radiopharmaceuticals, includes manufacturer's instructions that specify the method of preparation. FDA reviews and approves the information in the labeling to ensure that it accurately reflects the data on safety and effectiveness on which the drug approval is based. NRC has, in the past, relied primarily on FDA's determination of a drug's safety and effectiveness when it is prepared and used according to the approved labeling, which some NRC regulations refer to as the package insert, as one means of ensuring protection of the public health and safety.

NRC regulations in 10 CFR 35.200(b) require medical use licensees to prepare radiopharmaceuticals in accordance with the manufacturer's instructions in the package insert (a part of the FDA-approved labeling). Similar requirements are placed on commercial nuclear pharmacies through NRC license conditions. Regulations in 10 CFR 35.300, "Use of Radiopharmaceuticals for Therapy," require, among other things, that the licensees comply with the package insert instructions regarding indications and method of administration for the therapeutic use of radiopharmaceuticals.

II. Petition for Rulemaking Filed By The American College of Nuclear Physicians and the Society of Nuclear Medicine

On June 8, 1989, the NRC docketed as PRM-35-9 a petition for rulemaking dated June 5, 1989, which was filed by the American College of Nuclear Physicians and the Society of Nuclear Medicine (ACNP-SNM). The ACNP-SNM are composed of over 12,000 individuals who participate in the medical use of byproduct materials. Members include physicians, technologists, and nuclear

pharmacists. As characterized by the petitioners, the physicians supervise the preparation and administration of radiopharmaceuticals to diagnose and treat patients. Also, technologists administer radiopharmaceuticals to diagnose and perform clinical procedures under the direction and supervision of an authorized user physician.[2] Nuclear pharmacists reconstitute radiopharmaceutical kits, compound radiopharmaceuticals, and dispense radiopharmaceuticals for medical purposes.

Among other things,[3] the petitioners requested that the NRC amend its regulations at 10 CFR 35, "Medical Use of Byproduct Material," to recognize their appropriate practice of medicine and to allow (1) departures from the manufacturer's instructions for preparing diagnostic radiopharmaceuticals and (2) the use of radiopharmaceuticals for therapeutic indications and methods of administration not included in the package inserts approved by the FDA.

The petitioners stated that, under current NRC regulations, members of the petitioning organizations believe they cannot appropriately practice their professions. The petitioners also stated that authorized user physicians cannot prescribe certain radiopharmaceuticals or routes of administration for proper patient care, even though they believe they are permitted to do so by the FDA and by their State medical licenses. According to the petitioners, nuclear pharmacists have been disenfranchised as a professional entity because activities that they believe are permitted by the FDA and by the States are not allowed under NRC regulations. The petitioners stated that, although a nuclear pharmacist is authorized by State license to prepare radiopharmaceuticals upon receipt of a prescription by an authorized user physician, current NRC regulations severely restrict their activity. The petitioners believe that their professional activities are curtailed by the limitations imposed by the NRC on nuclear physicians and pharmacists.

A notice of receipt of the petition with a public comment period of 90 days was published in the Federal Register on September 15, 1989 (54 FR 38239). The Federal Register notice set forth the petitioners' proposed amendments to

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2 Whenever the term "authorized user physician" is used, it means the "authorized user" or the physician working under the supervision of the authorized user.

3 The NRC is working to resolve the remaining issues identified in the petition.

10 CFR Parts 30, 33, and 35, including the deletion of the restriction regarding the preparation of radiopharmaceuticals in § 35.200(b) and the deletion of the restriction in § 35.300, with respect to following the package insert instructions regarding indications and method of administration (54 FR 38240). The comment period closed on December 14, 1989, and 466 comment letters have been received.

Comments were received from many different sources such as hospitals, pharmacies, and medical associates. About 60 percent of the letters were similar to a form letter written for members of ACNP-SNM. These letters indicated agreement with the petition on all essential points. Fifteen percent of the comment letters were similar to a form letter written for the staff of Syncor International Corporation, also agreeing with the assertions in the petition. Twenty-five percent of the responses were letters from other individuals.

Most letters (99 percent) supported the petition and stated that the NRC should amend its regulations to relax its current restrictions on the practice of nuclear medicine and nuclear pharmacy. The majority of these letters did not provide specific supporting rationale. Some commenters provided rationale and examples of clinical cases that the commenters believe demonstrate how the relevant NRC regulations prevent physicians from providing proper care for their patients. The commenters stated that, although a licensee may request an exemption from specific requirements in the regulations on a case-by-case basis, this exemption process is time consuming and cumbersome. The commenters believe that a delay in order to obtain NRC approval for a particular departure from the package insert may, in some cases, jeopardize the patient's health. Some examples of clinical cases the commenters provided are described below:

(1) Licensees are not able to use Tc-99m macroaggregated albumin with high specific activity and low particle concentration to safely perform lung scans for patients who have pulmonary hypertension because the ranges of specific activity and particle concentration given in the package insert would be exceeded.

(2) Licensees are not able to add ascorbic acid as an antioxidant to Tc-99m-DTPA, which would increase stability and enhance image quality, because NRC regulations do not permit departure from the manufacturer's instructions for reconstituting reagent kits.

(3) When evaluating potential blood transfusions, licensees are not able to perform in vivo crossmatching using potential donor red cells radiolabeled with Tc-99m because this is not provided for in the package insert.

(4) Licensees are not able to use P-32 sodium phosphate to treat primary Thrombocythemia because this use is not specified in the package insert.

III. Need for a Rule.

Information submitted by the ACNP-SNM in the petition for rulemaking and obtained during subsequent discussions with licensees indicates that the requirements in § 35.200(b) regarding preparation of radiopharmaceuticals and in § 35.300 regarding indications and method of administration for therapy procedures are preventing authorized user physicians from providing certain nuclear medicine clinical procedures. License conditions similar to § 35.200(b) currently placed on commercial nuclear pharmacies have the same effect. For some uncommon disease states or patient conditions, in order to provide proper patient care, it may be necessary to depart from the FDA-approved instructions to obtain diagnostic or therapeutic medical results not otherwise attainable or to reduce medical risks to particular patients because of their medical condition.

The NRC believes that continued application of these restrictions governing the preparation of radiopharmaceuticals and the indications and the method of administration for therapeutic use of radiopharmaceuticals would not permit proper patient care to be provided to some patients.

Under its 1979 Medical Use Policy Statement (44 FR 8242, February 9, 1979), the NRC stated that it would regulate the medical use of byproduct material in order to protect the health and safety of workers, patients, and the public. In general, NRC regulatory requirements are oriented to ensure that the properly prepared radiopharmaceutical is administered to the correct patient as prescribed by an authorized user physician. Aside from the requirements in § 35.200(b) and § 35.300, other requirements in Part 35, such as the use of dose calibrators, are intended to ensure that the patient receives the prescribed dose. NRC's regulations need to provide a balance between adequate controls and avoidance of undue interference in medical judgments. The high level of public health and safety protection that accrues from following the FDA-approved instructions must be balanced with the need to

depart from those instructions to obtain diagnostic or therapeutic results not otherwise attainable or to reduce patient risk in some uncommon disease states or patient conditions in order to provide proper patient care.

The diagnostic use of radiopharmaceuticals is, in most cases, an area of inherently low radiation risk to patients (Policy Statement, 44 FR 8242; February 9, 1979). Although there are greater risks inherent in the use of therapeutic levels of radioactive drugs, in light of the information provided with and gathered subsequent to the petition, the NRC does not believe that limiting the therapeutic use of radiopharmaceuticals in all cases to only the indications and methods of administration specified in the package insert is justified. Moreover, as stated in its 1979 Policy Statement, the NRC recognizes that physicians have the primary responsibility for the protection of their patients. The Commission believes that basic decisions concerning the diagnosis and treatment of disease are a part of the physician-patient relationship and are traditionally considered to be part of the practice of medicine.

The NRC has made a determination that continued application of the subject requirements, without exceptions, may adversely affect the public health and safety because the delivery of proper patient care may require, in certain instances, that some radiopharmaceuticals be prepared and administered in a manner different from that stated in the FDA-approved instructions. The NRC has reviewed the information on nuclear medicine clinical procedures and believes that adequate protection of the public health and safety can be maintained while, at the same time, providing proper patient care. Hence, the NRC is issuing an interim final rule that permits, on the direction of an authorized user physician, departures from the manufacturer's instructions in preparing radiopharmaceuticals and departures from package inserts for indications and method of administration for therapeutic use, provided a proper record of the departure is made. These records will be examined by the NRC to determine whether to extend the interim period for the rule, make the rule permanent, or revise it based on the nature of, reasons for, and frequency of departures. The NRC will provide FDA the opportunity to review this information.

Because these amendments involve relief from restrictions which if left in place could have an adverse impact on public health and safety, and because the NRC has received and considered public comments on the petition for rulemaking,

good cause exists for omitting the notice of proposed rulemaking and the public procedures thereon as unnecessary and contrary to the public interest, and for making these amendments effective upon publication in the Federal Register without the customary thirty-day notice. This interim rule will terminate 3 years after the date of publication in the Federal Register.

IV. Future Agency Action.

This interim rule amending 10 CFR Parts 30 and 35 represents only one phase of NRC's resolution of the ACNP-SNM petition for rulemaking. During the 3-year period, the NRC may modify the interim rule or take other regulatory action it determines necessary to protect the public health and safety. Based on continued NRC analysis of the ACNP-SNM petition, the comments on the petition and on this interim rule, experience with the implementation of this interim rule, and other information, the NRC may propose amendments to this rule or to other provisions of 10 CFR Parts 30 and 35 as part of its resolution of all the issues raised in PRM-35-9.

V. Discussion.

§ 35.200 Use of radiopharmaceuticals, generators, and reagent kits for imaging and localization studies.

The NRC believes that persons licensed by the NRC to elute generators and prepare reagent kits should not always be bound by the requirement specified in 10 CFR 35.200(b) to follow the manufacturer's instructions for radiopharmaceuticals for which the FDA has approved an NDA. They should not be bound if they have a written directive (e.g., prescription) made by an authorized user physician directing a specific departure for a particular patient, or patients, or for a radiopharmaceutical, and which includes (1) the specific nature of the departure, (2) a precise description of the departure, and (3) a brief statement of the reasons why the departure from the manufacturer's instructions would obtain medical results not otherwise attainable or would reduce medical risks to particular patients because of their medical condition. The NRC recognizes that the physician may face severe time constraints during an emergency; therefore, an exception has been provided

in § 35.200(c). Under the exception, a written directive is not required before preparing the radiopharmaceutical if an authorized user physician determines that the delay in obtaining a written directive would jeopardize the patient's health. The written directive together with a statement of the emergency determination must be prepared within 3 working days of the emergency administration. The written directive and a record of the number of patient administrations under each departure must be retained by the licensee for a period of 5 years and made available for NRC inspection.

This interim rule does not address departures from "Investigational New Drug" (IND) generator elution instructions or IND protocol directions for reagent kit preparation because the departures may compromise the scientific integrity of the clinical investigation. Therefore, licensees must continue to follow the IND generator elution instructions and IND protocol directions for reagent kit preparation.

§ 35.300 Use of radiopharmaceuticals for therapy.

For a radiopharmaceutical for which the FDA has approved an NDA, the amendments to § 35.300 would permit a licensee, under certain circumstances, to use therapeutic radiopharmaceuticals for indications or a method of administration not specified in the package insert. Specifically, these uses would be permitted if an authorized user physician makes a record of the departure which includes the specific nature of the departure and a brief statement of the reasons why the departure would obtain medical results not otherwise attainable or would reduce medical risks to particular patients because of their medical condition. A record of the departures from indications and method of administration and a record of the number of patient administrations under each departure must be retained in an auditable form and be available for inspection for 5 years. If a kit or generator for a radiopharmaceutical for therapy were approved by FDA (through an NDA), this interim rule does not authorize departures from the manufacturer's instructions for eluting the generator or preparing the therapy kit.

§ 30.34 Terms and conditions of licenses.

Commercial nuclear pharmacies are licensed pursuant to 10 CFR Part 30, "Rules of General Applicability to Domestic Licensing of Byproduct Material." These licensees are required by a license condition similar to § 35.200(b) to elute generators and prepare reagent kits in accordance with the manufacturer's instructions. The NRC believes that authorized users obtaining radiopharmaceuticals from commercial nuclear pharmacy licensees should not be bound by this restriction in the commercial nuclear pharmacy license. Therefore, the NRC is amending 10 CFR 30.34, "Terms and Conditions of Licenses," to permit actions within the scope of those permitted by the new § 35.200(c). For situations not within the scope of the amended § 30.34, a commercial nuclear pharmacy licensee may file an application to have its license amended to permit specific departures from the manufacturer's instructions for identified products.

Under the interim rule, commercial nuclear pharmacy licensees would no longer be bound by the requirement in their licenses to follow the manufacturer's instructions for a radiopharmaceutical for which the FDA has approved an NDA if they have a written directive made by an authorized user physician directing a specific departure for a particular patient, or patients, or for a radiopharmaceutical, and which includes the specific nature of the departure, a precise description of the departure, and why the departure from the manufacturer's instructions would obtain medical results not otherwise attainable or would reduce medical risks to particular patients because of their medical condition. As in § 35.200(c), there is an exception to the requirement for a written directive before preparing the radiopharmaceutical in an emergency situation if an authorized user physician determines that a delay in obtaining the written directive would jeopardize the patient's health. In this case, the commercial nuclear pharmacy licensee shall obtain the written directive from the authorized user physician within 3 working days of the prescribed departure. The directive must contain information regarding the emergency and all other required information. Licensees shall keep those records in an auditable form and available for inspection for 5 years.

These amendments to § 30.34 take precedence over the restrictive conditions (i.e., on eluting generators and preparing reagent kits for NDA radiopharmaceuticals) in the licenses of commercial nuclear pharmacies.

Therefore, those parts of the license conditions no longer apply during the 3-year period when the interim rule is in effect. This interim rule does not address departures from IND generator elution instructions or IND protocol directions for reagent kit preparation, thus licensees shall continue to follow the IND instructions.

Continuing Applicability of Regulatory Requirements.

The NRC notes that this interim rule does not relieve licensees from the requirements to comply with other applicable NRC, FDA, and other Federal or State regulations or NRC orders or license conditions concerning possession or use of byproduct material for medical use or other purposes as specified in 10 CFR Parts 30, 32, 33, and 35. Moreover, if a radioactive biologic receives a product license approval (PLA), this interim rule does not authorize departures from the manufacturer's instructions for preparing the biologic. In addition, if a kit or generator for a radiopharmaceutical for therapy receives an approved NDA, this interim rule does not authorize departures from the manufacturer's instructions for eluting the generator or preparing the therapy kit. Neither of these approvals exists at this time and neither is authorized by current regulations.

Radiation Safety Responsibilities of Medical Use Licensees.

NRC medical use licensees are required by § 35.21 to appoint a Radiation Safety Officer (RSO) responsible for implementing the licensee's radiation safety program. The licensee is required, through the RSO, to ensure that radiation safety activities are being performed in accordance with approved procedures and regulatory requirements in the daily operation of the licensee's byproduct material program. Nothing in this rulemaking relieves the licensee from complying with the requirements of § 35.21.

In accordance with 10 CFR 35.22, NRC medical institution licensees are required to establish a Radiation Safety Committee (RSC) to oversee the use of byproduct material. The duties of the RSC are specified in § 35.22(b) and include reviews, on the basis of safety, of numerous aspects of a licensee's use of byproduct material. Nothing in this rulemaking relieves the licensee from complying with the requirements of § 35.22.

VI. Administrative Statements.

Finding of No Significant Environmental Impact: Availability

The Commission has determined under the National Environmental Policy Act of 1969, as amended, and the Commission's regulations in Subpart A of 10 CFR Part 51 that these amendments are not a major Federal action significantly affecting the quality of the human environment and therefore an environmental impact statement is not required. This interim rule amends NRC regulations to permit licensees who elute generators and prepare reagent kits to depart from the manufacturer's instructions if those persons have a written directive made by an authorized user physician that requests a specific departure for a particular patient, or patients, or for a radiopharmaceutical. This directive must provide the specific nature of the departure, a precise description of the departure, and the reasons why the departure from the manufacturer's instructions would obtain medical results, diagnostic or therapeutic, not otherwise attainable or would reduce medical risks to particular patients because of their medical condition. The amendment does not address departures from IND generator elution instructions or IND protocol directions for reagent kit preparation. The NRC is also modifying its regulations to permit, if certain requirements are met, the therapeutic use of radiopharmaceuticals without following the package instructions regarding indications and method of administration. The interim rule does not affect the exemption in 10 CFR Part 20 for the intentional exposure of patients to radiation for the purpose of medical diagnosis and therapy.

Although the rule may cause some patients to be exposed to higher or lower levels of radiation than otherwise expected, those exposures would be given to obtain medical results not otherwise attainable or to reduce other risks to the patient. It should be noted that current requirements do not limit the radiation dose prescribed by the authorized user physician for either diagnosis or therapy. The amendments would not relieve licensees from meeting the requirements in 10 CFR Parts 20 and 35 that restrict radiation exposure to medical care personnel in the restricted area or to the general public in the unrestricted area, or radioactive effluent releases. It is expected that there would be no significant change, either increase or decrease, in radiation

exposure to the public or to the environment beyond the exposures currently resulting from delivering the dose to the patient.

The Environmental Assessment and Finding of No Significant Impact is available for inspection at the NRC Public Document Room at 2120 L Street NW. (Lower Level), Washington, DC. Single copies of the Assessment are available from Dr. Tse (see ADDRESSES heading).

Paperwork Reduction Act Statement

This final rule amends information collection requirements that are subject to the Paperwork Reduction Act of 1980 (44 U.S.C. 3501 et seq.). These requirements were approved by the Office of Management and Budget approval numbers 3150-0010 and 3150-0017.

Public reporting burden for this collection of information is estimated to average .05 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to the Information and Records Management Branch (MNBB-7714), U.S. Nuclear Regulatory Commission, Washington, DC 20555; and to the Desk Officer, Office of Information and Regulatory Affairs, NEOB-3019, (3150-0017 and 3150-0010), Office of Management and Budget, Washington, DC 20503.

Regulatory Analysis

The Commission has prepared a regulatory analysis for these amendments. The analysis examines the benefits and impacts considered by the NRC. The regulatory analysis is available for inspection at the NRC Public Document Room at 2120 L Street NW. (Lower Level), Washington, DC. Single copies are available from Dr. Tse (see ADDRESSES heading).

The Commission requests public comments on the regulatory analysis. Comments are welcome at any time during the three-year period that the interim final rule is in effect. Comments on the analysis may be submitted to the NRC as indicated under the ADDRESSES heading.

Backfit Analysis

The NRC has determined that the backfit rule, 10 CFR 50.109, does not apply to these amendments because they do not involve any provisions that would impose backfits as defined in 10 CFR 50.109(a)(1).

List of Subjects

10 CFR Part 30

Byproduct material, Criminal penalty, Government contracts, Intergovernmental relations, Isotopes, Nuclear materials, Radiation protection, Reporting and recordkeeping requirements.

10 CFR Part 35

Byproduct material, Criminal penalty, Drugs, Health facilities, Health professions, Incorporation by reference, Medical devices, Nuclear materials, Occupational safety and health, Radiation protection, Reporting and recordkeeping requirements.

For the reasons set out in the preamble and under the authority of the Atomic Energy Act of 1954, as amended, the Energy Reorganization Act of 1974, as amended, and 5 U.S.C. 552 and 553, the NRC is proposing to adopt the following amendments to 10 CFR Parts 30 and 35.

PART 30 -- RULES OF GENERAL APPLICABILITY TO DOMESTIC LICENSING OF BYPRODUCT MATERIAL

1. The authority citation for Part 30 is revised to read as follows:

Authority: Secs. 81, 82, 161, 182, 183, 186, 68 Stat. 935, 948, 953, 954, 955, as amended, sec. 234, 83 Stat. 444, as amended (42 U.S.C. 2111, 2112, 2201, 2232, 2233, 2236, 2282); secs. 201, as amended, 202, 206, 88 Stat. 1242, as amended, 1244, 1246 (42 U.S.C. 5841, 5842, 5846).

Section 30.7 also issued under Pub. L. 95-601, sec. 10, 92 Stat. 2951 (42 U.S.C. 5851). Section 30.34(b) also issued under sec. 184, 68 Stat. 954, as

amended (42 U.S.C. 2234). Section 30.61 also issued under sec. 187, 68 Stat. 955 (42 U.S.C. 2237).

For the purposes of sec. 223, 68 Stat. 958, as amended (42 U.S.C. 2273); §§ 30.3, 30.34(b),(c), (f), (g), and (i), 30.41(a) and (c), and 30.53 are issued under sec. 161b, 68 Stat. 948, as amended (42 U.S.C. 2201(b)); and §§ 30.6, 30.9, 30.34(g), 30.36, 30.51, 30.52, 30.55, and 30.56(b) and (c) are issued under sec. 161o, 68 Stat. 950, as amended (42 U.S.C. 2201(o)).

2. In § 30.34, paragraph (i) is added to read as follows:

§ 30.34 Terms and conditions of licenses.

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(i)(1) From [insert date of publication] to [insert date 3 years from the date of publication], each licensee eluting generators and processing radioactive material with diagnostic reagent kits for which the Food and Drug Administration (FDA) has approved a "New Drug Application" (NDA) may depart from the manufacturer's elution and preparation instructions (for radiopharmaceuticals authorized for use pursuant to § 35.200) provided that:

(i) The licensee has a written directive made by an authorized user physician that directs a specific departure for a particular patient, or patients, or for a radiopharmaceutical, and which includes the specific nature of the departure, a precise description of the departure, and a brief statement of the reasons why the departure from the manufacturer's instructions for preparing the radiopharmaceutical would obtain medical results not otherwise attainable or would reduce medical risks to particular patients because of their medical condition. The licensee shall keep the written directive and record of the number of prescriptions dispensed under the departure in an auditable form and available for inspection for 5 years; or

(ii) An authorized user physician determines, in accordance with § 35.200(c), that a delay in preparing the radiopharmaceutical in order to make a written directive would jeopardize the patient's health because of the emergent nature of the patient's medical condition. In this case, the licensee shall obtain the written directive made by the authorized user physician which contains the notation regarding the emergency and all the information specified in paragraph (i)(1)(i) of this section within 3 working days after the

prescribed departure. The licensee shall keep these records in an auditable form and available for inspection for 5 years.

(2) The actions authorized in paragraph (i)(1) of this section are permitted notwithstanding more restrictive language in license conditions unless those license conditions specifically reference § 30.34(i).

(3) Nothing in this section relieves the licensee from complying with other applicable NRC, FDA, and other Federal or State regulations governing the elution of generators and preparation of reagent kits.

PART 35 - MEDICAL USE OF BYPRODUCT MATERIAL

3. The authority citation for Part 35 is revised to read as follows:

Authority: Secs. 81, 161, 182, 183, 68 Stat. 935, 948, 953, 954, as amended, (42 U.S.C. 2111, 2201, 2232, 2233); sec. 201, 88 Stat. 1242, as amended (42 U.S.C. 5841).

For the purposes of sec. 223, 68 Stat. 958, as amended (42 U.S.C. 2273); §§ 35.11, 35.13, 35.20 (a) and (b), 35.21 (a) and (b), 35.22, 35.23, 35.25, 35.27 (a), (c) and (d), 35.31 (a), 35.49, 35.50 (a)-(d), 35.51 (a)-(c), 35.53 (a)-(b), 35.59 (a)-(c), (e)(1), (g) and (h), 35.60, 35.61, 35.70(a)-(f), 35.75, 35.80 (a)-(e), 35.90, 35.92 (a), 35.[illegible]0, 35.200 (b) and (c), 35.204 (a) and (b), 35.205, 35.220, 35.300, 35.310 [illegible], 35.315, 35.320, 35.400, 35.404 (a), 35.406 (a) and (c), 35.410 (a), 35.41[illegible], 35.420, 35.500, 35.520, 35.605, 35.606, 35.610 (a) and (b), 36.615, 35.620, 35.630 (a) and (b), 35.632 (a)-(f), 35.634 (a)-(e), 35.636 (a) and (b), 35.641 (a) and (b), 35.643 (a) and (b), 35.645 (a) and (b), 35.900, 35.910, 35.920, 35.930, 35.932, 35.934, 35.940, 35.941, 35.950, 35.960, 35.961, 35.970, and 35.971, are issued under sec. 161b, 68 Stat. 948, as amended (42 U.S.C. 2201(b)); and §§ 35.14, 35.21 (b), 35.22 (b), 35.23 (b), 35.27 (a) and (c), 35.29 (b), 35.33 (a)-(e), 35.36 (b), 35.50 (e), 35.51 (d), 35.53 (c), 35.59 (d) and (e)(2), 35.59 (g) and (i), 35.70 (g), 35.80 (f), 35.92 (b), 35.200 (c), 35.204 (c), 35.300 (b), 35.310 (b), 35.315 (b), 35.404 (b), 35.406 (b) and (d), 35.410 (b), 35.415 (b), 35.610 (c), 35.615 (d)(4), 35.630 (c), 35.632 (g), 35.634 (f), 35.636 (c), 35.641 (c), 35.643 (c), 35.645, and 35.647 (c) are issued under sec. 161o, 68 Stat. 950, as amended (42 U.S.C. 2201(o)).

4. In § 35.8, paragraph (b) is revised to read as follows:

§ 35.8 Information Collection Requirements: OMB approval.

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(b) The approved information collection requirements contained in this part appear in §§ 35.12, 35.13, 35.14, 35.21, 35.22, 35.23, 35.27, 35.29, 35.31, 35.33, 35.50, 35.51, 35.53, 35.59, 35.60, 35.61, 35.70, 35.80, 35.92, 35.200, 35.204, 35.205, 35.300, 35.310, 35.315, 35.404, 35.406, 35.410, 35.415. 35.606, 35.610, 35.615, 35.630 35.632, 35.634, 35.636, 35.641, 35.643, 35.645, and 35.647.

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5. In § 35.200, paragraph (c) is added to read as follows:

.200 Use of radiopharmaceuticals, generators, and reagent kits for imaging an .ocalization studies.

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(c)(1) From [insert date of publication] to [insert date 3 years from the date of publication], a licensee may depart from the manufacturer's instructions for eluting generators and preparing reagent kits for which FDA has approved an NDA, provided that the licensee has a written directive made by an authorized user physician that directs a specific departure for a particular patient, or patients, or for a radiopharmaceutical, and which includes the specific nature of the departure, a precise description of the departure, and a brief statement of the reasons why the departure from the manufacturer's instructions for preparing the radiopharmaceutical would obtain medical results not otherwise attainable or would reduce medical risks to particular patients because of their medical condition. If the authorized user physician determines that a delay in preparing the radiopharmaceutical in order to make a written directive would jeopardize the patient's health because of the emergency nature of the patient's medical condition, the radiopharmaceutical may be prepared without first making a written directive. The authorized user physician shall make notation of this determination in the written directive within 3 working days after the prescribed departure.

(2) The licensee shall keep the written directive and a record of the number of patient administrations under the departure in an auditable form and available for inspection for a perind of 5 years.

(3) Nothing in this section relieves the licensee from complying with other applicable NRC, FDA, and other Federal or State regulations governing the elution of generators and preparation of reagent kits.

6. In § 35.300, the existing text is designated as paragraph (a) and a new paragraph (b) is added to read as follows:

§ 35.300 Use of radiopharmaceuticals for therapy.

* * * * *

(b)(1) From [insert date of publication] to [insert date 3 years from the date of publication], a licensee may depart from the package insert instructions regarding indications or method of administration for a radiopharmaceutical for which FDA has approved an NDA, provided that the authorized user physician makes a record of the departure which includes the specific nature of the departure and a brief statement of the reasons why the departure would obtain medical results not otherwise attainable or would reduce medical risks to particular patients because of their medical condition. Licensees are not authorized to depart from the manufacturer's instructions for eluting a generator or preparing any kit for a radiopharmaceutical for therapy.

(2) The licensee shall obtain this record within 3 working days of the administration and keep this record and a record of the number of patient administrations under the departure in an auditable form and available for inspection for 5 years.

(3) Nothing in this section relieves the licensee from complying with other applicable NRC, FDA (including requirements governing the submission of an IND), and other Federal or State regulations governing the use of radiopharmaceuticals for therapy.

Dated at Rockville, Maryland, this 17th day of August, 1990.

For the Nuclear Regulatory Commission.

Samuel J. Chilk,
Secretary of the Commission.