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DEC 11 1984

MEMORANDUM FOR: William S. Olmstead, Director
Regulations Division, ELD

Karl R. Goller, Director
Division of Radiation Programs and
Earth Sciences, RES

John D. Philips, Chief
Rules and Procedures Branch, ADM

FROM: Richard E. Cunningham, Director
Division of Fuel Cycle and Material Safety

SUBJECT: REQUEST FOR CONCURRENCE ON PROPOSED RULEMAKING TO AUTHORIZE ADDITIONAL METHODS OF USE FOR APPROVED RADIOPHARMACEUTICALS

Attached for your concurrence is a proposed rulemaking that would amend 35.14(b)(7) of 10 CFR Part 35, "Human Uses Of Byproduct Material." The proposed rule is in accordance with NRC's policy as described in the Federal Register on February 3, 1983 (48 FR 5217).

This proposed rulemaking would amend the regulations to allow licensees to use the following FDA-approved drugs for the following new methods of use: technetium-99m labeled sulfur colloid for gastroesophageal imaging; technetium-99m labeled sulfur colloid, pertechnetate, or macroaggregated human serum albumin for LeVeen, ventriculo-atrial, and ventriculo-peritoneal shunt imaging; and technetium-99m labeled pertechnetate for cystography and dacryocystography.

Cognizant individuals for this proposed rulemaking are Thomas Dorian, ELD, Judy Foulke, RES, and Michael Lesar, ADM.

Please review the enclosures and submit your concurrence to me by DEC 28 1984.

Richard E. Cunningham, Director
Division of Fuel Cycle and
Material Safety

Enclosures:
1. Federal Register Notice Package
2. 48 FR 5217

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RECunningham
12/ /84

*See previous concurrence

FCML	*FCML	*FCML	ELD	RES	ADM	DD/FC
CMcDonald:ht	NMcElroy	VLMiller	TDorian	JFoulke	MLesar	DRChapell
12/05/84	12/05/84	12/05/84	12/ /84	12/ /84	12/ /84	12/ /84

DRAFT

MEMORANDUM FOR: William J. Dircks
Executive Director for Operations

FROM: John G. Davis, Director
Office of Nuclear Material Safety and Safeguards

SUBJECT: AMENDMENT TO 10 CFR 35.14(b)(7) TO ALLOW USE OF CERTAIN RADIOPHARMACEUTICALS FOR PROCEDURES NOT LISTED ON THE FDA-APPROVED LABELS

Attached for your signature is a proposed rulemaking that would amend 35.14(b)(7) of 10 CFR Part 35, "Human Uses Of Byproduct Material."

The purpose of this proposed amendment is to allow physicians or hospitals that are now permitted by NRC to use other radiopharmaceuticals to use certain radiopharmaceuticals for recently developed methods of use not listed on their respective package labels. The amendment will reduce NRC and licensee administrative costs by eliminating the need for licensees to request a license amendment if they want to use a radiopharmaceutical for a new method of use.

Currently, if a physician uses a radiopharmaceutical approved by the Food and Drug Administration (FDA) for a method of use not listed on the package label, the physician is required by NRC regulation to follow the label instructions for (1) chemical and physical form, (2) route of administration, and (3) dosage range. Physicians who use radiopharmaceuticals for the methods of use listed in §35.14(b)(7) of 10 CFR Part 35, "Human Uses of Byproduct Material," are excepted from this requirement. This regulatory policy is described in an NRC Federal Register notice published on February 3, 1983 (48 FR 5217).

This proposed rulemaking would amend §35.14(b)(7) to allow licensees to use the following FDA-approved drugs for the following new methods of use: technetium-99m labeled sulfur colloid for gastroesophageal imaging; technetium-99m labeled sulfur colloid, pertechnetate, or macroaggregated human serum albumin for LeVeen, ventriculo-atrial, and ventriculo-peritoneal

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shunt imaging; and technetium-99m labeled pertechnetate for cystography and dacryocystography.

The Office of the Executive Legal Director has no legal objection and the Offices of Administration and Nuclear Regulatory Research concur in the amendment to 10 CFR Part 35.14(b)(7).

John G. Davis, Director
Office of Nuclear Material
Safety and Safeguards

Enclosures:
1. Federal Register Notice
2. Federal Register Notice (48 FR 5217)

DEC 11 1984 DRAFT

Approved For Publication

In a final rule published March 19, 1982 (47 FR 11816), the Commission delegated to the Executive Director for Operations (10 CFR 1.40(c) and (d)) the authority to develop and romulgate rules as defined in the APA (5 U.S.C. 551(4)), subject to the limitations in NRC Manual Cnapter 0103, Organization and Functions, Office of the Executive Director for Operations, paragraphs 0213, 038, 039, and 0310.

The proposed rule entitled "Physician's Use of Radioactive Drugs," would amend 10 CFR 35.14(b)(7) to allow licensees to use certain radiopharmaceuticals for recently developed methods of use not listed on their respective labels.

This final rule does not constitute a significant question of policy, nor does it amend regulations contained in 10 CFR Parts 0, 2, 7, 8, 9 Subpart C or 110. I, therefore, find that this rule is within the scope of my rulemaking authority and am proceeding to issue it.

_____
Date

_____
William J. Dircks
Executive Director
for Operations

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DEC 11 1984

WEEKLY REPORT TO THE COMMISSION

OFFICE OF NUCLEAR MATERIAL SAFETY AND SAFEGUARDS

Proposed Rule to be Signed by EDO

On _____, 1984, the Executive Director for Operations approved a proposed rule that would amend 10 CFR Part 35, "Human Uses of Byproduct Material," by allowing licensees to use the following FDA-approved drugs for the following clinical procedures: technetium-99m labeled sulfur colloid for gastroesophageal imaging; technetium-99m labeled sulfur colloid, pertechnetate, or macroaggregated human serum albumin for LeVeen, ventriculo-atrial, and ventriculo-pertioneal shunt imaging; and technetium-99m labeled pertechnetate for cystography and dacryocystography. This action is taken pursuant to NRC policy published in the Federal Register on February 4, 1983 (48 FR 5217).

This notice constitutes notice to the Commission that, in accordance with the rulemaking authority delegated to the EDO, the EDO has received this proposed rule and proposes to forward it on _____ to the Secretary for Federal Register publication.

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ENVIRONMENTAL IMPACT ASSESSMENT FOR AMENDMENT TO 35.14(b)(7) OF 10 CFR PART 35 TO PERMIT MEDICAL LICENSEES TO USE CERTAIN RADIOPHARMACEUTICALS FOR PROCEDURES NOT LISTED ON THE FDA-APPROVED LABEL

Introduction:

Physicians who want to use certain radioactive materials in the practice of medicine may do so only in accordance with a license issued by the Nuclear Regulatory Commission (NRC) or an Agreement State. Physicians are required by NRC regulation to use drugs in accordance with package label instructions approved by the Food and Drug Administration (FDA). The NRC is proposing to amend its regulations to provide an exception that would allow physicians to use certain approved drugs for methods of use not yet approved by FDA.

Procedure Descriptions:

1. Technetium-99m sulfur colloid is used as a diagnostic imaging agent for the liver, spleen, and bone marrow. It can also be used as proposed for gastroesophageal imaging. When administered orally either as solid or liquid test meal, technetium-99m sulfur colloid permits external imaging that is helpful in assessing gastric emptying, gastroesophageal reflux, and esophageal transit.

2. A LeVeen shunt is an implanted tube that drains built-up fluid from the peritoneal cavity to a large central vein. Technetium-99m labeled sulfur colloid, pertechnetate, or macroaggregated human serum albumin can be injected into the peritoneal cavity to diagnose shunt malfunction, such as blockage by clot or valve failure, by taking images of the shunt.

3. A ventriculo-atrial shunt is a tube implanted in patients with hydrocephalus (fluid build-up in the head). It drains the fluid from the head to the atrial cavity. Technetium-99m labeled sulfur colloid, pertechnetate, or macroaggregated human serum albumin is injected into the shunt system of the patient to localize shunt blockage before surgical repair is performed.

4. A ventriculo-peritoneal shunt is an implanted tube in patients with hydrocephalus (fluid build-up in the head). It drains the fluid from the head to the peritoneal cavity. Technetium-99m labeled sulfur colloid, pertechnetate, or macroaggregated human serum albumin is injected into the shunt system of patients to localize shunt blockage before performing surgical repairs.

5. Cystography is a procedure for patients with bladder problems. A tube is inserted into the bladder of a patient. Technetium-99m pertechnetate is instilled through the tube into the bladder. Images are taken during filling and voiding of the bladder to measure the actual amount of reflux (backward flow) into the upper tracts, to quantitate bladder volume at which reflux occurs, to calculate drainage time of reflux after voiding, and the remaining urine volume.

6. Dacryocystography is a procedure for patients who exhibit excessive teardrop problems (epiphora). Technetium-99m labeled pertechnetate is administered as a sterile eye drop. This procedure is performed to assess tear production and drainage in patients, and for nasolacrimal system imaging.

Need for the Proposal:

As new uses for FDA-approved drugs are developed, NRC considers amending its regulations to provide physicians an exception from its requirement to only use a radiopharmaceutical for the methods of use listed on the package label (see 48 FR 5212). This facilitates potentially beneficial new uses of approved drugs.

Alternatives:

Proposed Action: By amending the Commission's rules, provide an exception that would allow physicians to use the approved radiopharmaceuticals for the new uses.

Alternative: No action. (Licensees could individually ask that these additional uses for approved drugs be specifically authorized on their respective licenses.)

Impact:

Without this exception, a licensee authorized to use these drugs for approved uses could not use them for the excepted procedures in patients who, in the physician's judgment, should receive them for diagnostic imaging. The NRC licensing process assures that appropriately trained physicians with adequate facilities, radiation safety training and program control will use these drugs safely in medical practice.

Concerning radiation exposure of the ecosystem, the Commission notes that a National Academy of Sciences-National Research Council Committee has found that "Evidence to date indicates that probably no other living organisms are very much more radiosensitive than man so that if man as an individual is protected, then other organisms and populations would be most unlikely to suffer harm." ("The Effects on Populations of Exposure to Low Levels of Ionizing Radiation," National Academy of Sciences-National Research Council, Washington, D.C. 20006, November 1972, p. 34). Because the radiopharmaceuticals will be used by persons with training and experience, facilities and equipment, and radiation safety procedures found adequate to keep exposures within the limits of 10 CFR Part 20, the Commission has determined that significant human impact is unlikely. Similarly, any detectable effect on other living organisms or the quality of the human environment is unlikely.

Summary and Conclusion

The alternative and proposed action both permit use of the drugs by physicians adequately trained to use them safely. The proposed action is preferred over the alternative for reasons of administrative convenience which have no bearing on environmental impact. The proposed action will not have any significant environmental impact.

References:

1. Revised Training and Experience Criteria for Nuclear Medicine Physicians (47 FR 54367) dated December 2, 1982.
2. "The Effects on Populations to Exposure to Low Levels of Ionizing Radiation," National Academy of Sciences-National Research Council, Washington, D.C. 20006, November, 1972.

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REGULATORY ANALYSIS FOR AMENDMENT OF 10 CFR 35.14(b)(7) TO ALLOW USE OF CERTAIN RADIOPHARMACEUTICALS FOR PROCEDURES NOT LISTED ON THE FDA-APPROVED LABEL

1. Statement of the Problem

If a physician uses a radiopharmaceutical approved by the Food and Drug Administration (FDA) for a method of use not identified on the package labeling, the physician is required by NRC regulation to follow the labeling instructions for (1) chemical and physical form, (2) route of administration, and (3) dosage range. Physicians who use radiopharmaceuticals for the methods of use listed in §35.14(b)(7) of 10 CFR Part 35, "Human Uses of Byproduct Material," are excepted from this requirement. The purpose of this proposed amendment is to add some recently developed methods of use to that section. This regulatory policy is described in an NRC Federal Register notice published on February 4, 1983 (48 FR 5217).

2. Objectives

The proposed regulatory action is designed to allow physicians or hospitals that are now permitted by NRC to use other radiopharmaceuticals to use these radiopharmaceuticals for methods of use not listed on their respective labels. The amendment will reduce administrative costs by eliminating the need for licensees to request a license amendment if they want to use a radiopharmaceutical for a listed method of use.

3. Alternatives

Proposed Action: Add the drugs and methods of use to §35.14(b)(7) by amending the Commission's regulations.

Alternative 1: No action. (Licensees could individually ask that these additional uses be specifically authorized on their respective licenses.)

Alternative 2: Ask FDA to change the approved labeling to include the new method of use.

4. Consequences

Proposed Action: This proposed rule would relieve a majority of NRC's medical licensees from certain regulatory requirements. All affected licensees would be able to use the radiopharmaceuticals for the listed methods of use without the cost and delay associated with a license amendment.

Alternative 1: Alternative 1 would require each of the approximately 1900 medical licensees who may want to use the radiopharmaceuticals for the listed methods of use to request a license amendment. Each amendment would cost the licensee $230 of administrative and clerical effort (estimated at about 2 to 5 hours of licensee effort to prepare paperwork) plus the $120 NRC license amendment fee. The total cost to each licensee would be approximately $350. A large number of amendment requests would create an unacceptable backlog in the licensing section.

Alternative 2: This alternative would default to the no action alternative because FDA will not initiate a label change of its own volition; a request for a change in approved labeling must be initiated by the manufacturer of the radiopharmaceutical. We assume the manufacturers believe that the few additional sales that would result from the new methods of use would not be sufficient to cover the expense of preparing the requests for label change; otherwise, they would have requested the label changes.

5. Decision Rationale

The proposed action is recommended because it requires no costs to licensees, and will not consume extensive NRC staff resources. In addition, it provides an opportunity for public comment which would not be provided by Alternative 1.

Alternative 1 is not recommended because individual licensing actions would involve considerable delay and unnecessary expense to licensees. Also, NRC does not have the technical and clerical resources needed to promptly process the large number of amendment requests that might be received.

Alternative 2 is not recommended because manufacturers have insufficient motive to shoulder the burden of preparing the necessary requests for label changes.

6. Implementation

The staff will prepare supporting documents and publish a proposed rule in the Federal Register. The staff, with assistance from the Advisory Committee on the Medical Uses of Isotopes, will analyze the public comments received and prepare a final rule. The Office of Administration will mail copies of the proposed and final rule to affected licensees.

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NUCLEAR REGULATORY COMMISSION

10 CFR PART 35

Physician's Use of Radioactive Drugs

AGENCY: Nuclear Regulatory Commission.

ACTION: Proposed rule.

SUMMARY: The Nuclear Regulatory Commission (NRC) is proposing to amend its regulations to allow physicians to use technetium-99m labeled sulfur colloid for gastroesophageal imaging; technetium-99m labeled sulfur colloid, pertechnetate, and macroaggregated human serum albumin for LeVeen, ventriculo-atrial and ventriculo-peritoneal shunt imaging; and technetium-99m labeled pertechnetate for cystography and dacryocystography. Without this amendment, each NRC licensee that wants to use these radioactive materials in these ways would have to apply to the NRC for permission to do so. The proposed rule will allow physicians or hospitals that are now licensed by NRC to use other similar materials to use these drugs without making an application to NRC.

DATE: Comment period expires [***30 days from date of publication***] Comments received after this date will be considered if it is practical to do so, but assurance of consideration cannot be given except as to comments received on or before this date.

ADDRESSES: Send comments to: The Secretary of the Commission, U.S. Nuclear Regulatory Commission, Washington, DC 20555, ATTN: Docketing and Service Branch. Hand deliver comments to: Room 1121, 1717 H Street, NW, Washington, DC between 8:15 am and 5:00 pm. Examine comments received, environmental and regulatory analyses and the requests for exception at: The NRC Public Document Room, 1717 H Street, NW, Washington, DC.

FOR FURTHER INFORMATION CONTACT: Norman L. McElroy, Office of Nuclear Material Safety and Safeguards, U.S. Nuclear Regulatory Commission, Washington, DC 20555, Telephone: (301) 427-4108.

SUPPLEMENTARY INFORMATION: Physicians who want to use certain radioactive materials in the practice of medicine may do so only in accordance with a license issued by the Nuclear Regulatory Commission (NRC) or by States which have an agreement with the NRC to license the use of these materials instead of the NRC.

As new radiopharmaceuticals, radioactive sources, medical devices, and uses of radioisotopes are developed, the NRC considers adding them to one of the groups under which medical licenses are issued. The groups were designed to allow physicians and community hospitals wide access to nuclear medicine services. The groups in §35.100 contain only radiopharmaceuticals that are the subject of an FDA-approved "New Drug Application" (NDA), or a "Notice of Claimed Investigational Exemption for a New Drug" (IND) that has been accepted by FDA. A licensee authorized to use all the materials listed in a group is referred to as a "group medical licensee."

NRC regulations in §35.14(b)(6) that apply to the group medical licensees provide that when a physician uses byproduct material for clinical procedures other than those approved by FDA and specified in the product labeling or package insert, the physician must follow the product labeling regarding: (1) chemical and physical form, (2) route of administration, and (3) dosage range. The NRC has received requests to amend its regulations to provide an exception from the product labeling requirement for technetium-99m sulfur colloid when used for gastroesophageal imaging; technetium-99m labeled sulfur colloid, pertechnetate, and macroaggregated human serum albumin when used for LeVeen, ventriculo-atrial, and ventriculo-peritoneal shunt imaging; and technetium-99m labeled pertechnetate for cystography and dacryocystography. These are clinical procedures that are not listed in the product labels.

It is noteworthy that NRC and FDA have sought a solution to the general problem of drug labeling, and FDA currently is considering a program to authorize additional clinical procedures that use approved radiopharmaceuticals. However, until such a program is implemented, NRC believes that this rulemaking is the most appropriate way to resolve the problem in this interim period. This policy was described in an NRC rulemaking published in the Federal Register on February 3, 1983 (48 FR 5217).

The requests for exception that NRC received provided a description of the clinical procedure, a justification for the exception, the purpose of the procedure, an analysis of the radiation dose, and additional technical and scientific information. (Each of the requests for exception is available for inspection at the NRC Public Document Room, 1717 H Street, NW, Washington, D.C.) The NRC has reviewed the requests to determine whether the requested exception from the requirements in §35.14(b)(6) might result in an unreasonable risk to the health and safety of the public or might endanger life or property. The NRC specifically considered two criteria:

- No unjustified radiation dose to the patient, and
- Demonstration of adequacy of occupational radiation protection measures

With assistance from its Advisory Committee on the Medical Uses of Isotopes (ACMUI), the NRC has determined that the above criteria have been met for the proposed clinical procedures. Many of the committee members believe that these clinical procedures are useful, and the risk/benefit ratio for these procedures is extremely low. They also noted that these techniques will probably become routine once approved by NRC.

Technetium-99m labeled sulfur colloid can be administered orally either as a solid or liquid test meal. Following oral administration, technetium-99m sulfur colloid goes from the esophagus to the stomach, small intestine, and the upper large intestine. This clinical procedure permits external imaging which is helpful in assessing gastric emptying, gastroesophageal reflux, and esophageal transit. The gastric emptying procedure is useful in demonstrating the presence and the severity of gastric motor disorder; the gastroesophageal reflux study may demonstrate backward flow in the digestive tract. The esophageal transit study may demonstrate obstructions or abnormal transit time. The radiation dose to an average adult patient from 1 millicurie of orally administered technetium-99m sulfur colloid as a liquid is: 0.1 rad to the stomach wall; 0.3 rad to the small intestine; 0.5 rad to the upper large intestine; 0.3 rad to the lower large intestine; 0.1 rad to the ovaries; 0.01 rad to the testes; and 0.02 rad to the whole body. The estimated absorbed radiation dose to an average adult patient from 1 millicurie of orally administered technetium-99m sulfur colloid as a solid food is: 0.2 rad to the stomach wall; 0.2 rad to the small intestine; 0.4 rad to the upper large intestine; 0.3 rad to the lower large intestine; 0.1 rad to the ovaries, 0.004 rad to the testes; and 0.02 rad to the whole body.

These estimated absorbed radiation doses and the following doses are similar to other absorbed doses received from diagnostic nuclear medicine and x-ray procedures.

A LeVeen shunt is an implanted tube that drains built-up fluid from the peritoneal cavity to a large central vein. Technetium-99m labeled sulfur colloid, pertechnetate, or macroaggregated human serum albumin can be injected into the peritoneal cavity to diagnose shunt malfunction, such as blockage by clot or valve failure, by taking images of the shunt. The normal dosage is 3 to 10 millicuries. The radiation dose from an intraperitoneal injection of a 3 millicurie dosage of technetium-99m sulfur colloid is: 0.02 rad to the whole body; 0.02 rad to the testes; 0.02 rad to the ovaries; 0.03 rad to the liver; 0.02 rad to the spleen and 0.03 rad to the red marrow.

A ventriculo-atrial shunt is a tube implanted in patients with hydrocephalus (fluid build-up in the head). It drains the fluid from the head to the atrial cavity. Technetium-99m labeled sulfur colloid, pertechnetate, or macroaggregated human serum albumin is injected into the shunt system of the patient to localize shunt blockage before surgical repair is performed. The normal dosage is 1 to 5 millicuries. The radiation dose from an injection of a 5 millicurie dosage of technetium-99m to a patient with a patent shunt is: 0.1 rad to the whole body and 0.1 rad to the brain.

A ventriculo-peritoneal shunt is an implanted tube in patients with hydrocephalus (fluid build-up in the head). It drains the fluid from the head to the peritoneal cavity. Technetium-99m labeled sulfur colloid, pertechnetate, or macroggregated human serum albumin is injected into the shunt system of patients to localize shunt blockage before performing surgical repairs. The normal dosage is 1 to 5 millicuries. The radiation dose from an injection of a 5 millicurie dosage of technetium-99m to a patient with a patent shunt is: 0.1 rad to the whole body and 0.1 rad to the brain.

Cystography is a procedure for patients with bladder problems. A tube is inserted into the bladder of a patient. Technetium-99m pertechnetate is instilled through the tube into the bladder. Images are taken during filling and voiding of the bladder to measure the amount of reflux (backward flow) into the upper tracts, bladder volume at which reflux occurs, drainage time of reflux after voiding, and the remaining urine volume. The normal dosage is 1 millicurie. The radiation dose from a 1 millicurie dosage of technetium-99m pertechnetate is: 0.002 rad to the whole body, 0.006 rad to gonads, and 0.2 rad to the bladder.

Dacryocystography is a procedure for patients whose eyes exhibit excessive teardrops (epiphora). This procedure is performed to assess tear production and drainage in patients, and for nasolacrimal system imaging. Technetium-99m labeled pertechnetate is administered as a sterile eye drop. The normal dosage is 100 to 250 microcuries. The radiation dose from a dosage of 100 to 150 microcuries of technetium-99m pertechnetate per eye drop to the germinal epithelium of the lens is: 0.01 to 0.02 rad under normal physiological conditions. With blocked lacrimal drainage, the dose to the lens is 0.4 to 0.6 rad.

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 this is not a major Federal action significantly affecting the quality of the human environment and therefore an environmental impact statement is not required. The assessment shows that any detectable effect on the environment is unlikely. The environmental assessment and finding of no significant impact on which this determination is based are available for inspection at the NRC Public Document Room, 1717 H Street, NW, Washington, DC. Single copies of the environmental assessment are available from Mr. McElroy (see "For Further Information Contact" heading).

Paperwork Reduction Act Statement

This proposed rule contains no information collection requirements and therefore it is not subject to the requirements of the Paperwork Reduction Act of 1980 (44 U.S.C. 3501 et. seq.).

Regulatory Analysis

The NRC has prepared a draft regulatory analysis for this proposed rule. The analysis examines the costs and benefits of the alternatives considered by the NRC. The draft analysis is available for inspection at the NRC Public Document Room, 1717 H Street, NW, Washington DC. A single copy may be obtained from Mr. McElroy (see "For Further Information Contact" heading).

Regulatory Flexibility Certification

As required by the Regulatory Flexibility Act of 1980, 5 U.S.C. 605 (b), the NRC certifies that this rule, if adopted, will not have a significant economic impact on a substantial number of small entities. The NRC has prepared a draft regulatory analysis for this proposed rule that examines the economic impact of this action. The analysis notes that approximately 1900 medical licensees may experience some beneficial impact from the rule. The proposed rule would spare each medical licensee, desiring to use the radioactive material in the requested manner, the estimated $230 cost of preparing a license amendment request, the $120 amendment fee, and the delay (length and cost undetermined) associated with the amendment of the license.

The Commission is seeking comment particularly from small entities (i.e., small businesses, small organizations, and small jurisdictions as defined by the Regulatory Flexibility Act) about the ways the proposed rule will affect them and the ways it may be modified to impose less stringent requirements on them which will still adequately protect the public health and safety. Those small entities that offer comments on how the regulations could be modified to take into account their differing needs should specifically discuss:

(a) The size of their business and how the proposed regulations would result in a significant economic burden upon them as compared to larger organizations in the same business community;

(b) How the proposed regulation could be modified to take into account their differing needs or capabilities;

(c) The benefits that would accrue, or the detriments that would be avoided, if the proposed regulation were modified as suggested by the commenter;

(d) How the proposed regulation, as modified, would more closely equalize the impact of NRC regulations or create more equal access to the benefits of Federal programs as opposed to providing special advantages to any individuals or groups; and

(e) How the proposed regulation, as modified, would still adequately protect the public health and safety.

List of Subjects in 10 CFR Part 35

Byproduct material, Drugs, Health facilities, Health professions, Incorporation by reference, Medical devices, Nuclear materials, Occupational safety and health, Penalty, 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. 553, the following amendment to 10 CFR Part 35 is being considered.

PART 35 - HUMAN USES OF BYPRODUCT MATERIAL

1. The authority citation for Part 35 continues 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); §§35.2, 35.14(b), (e) and (f), 35.21(a), 35.22(a), 35.24, and 35.31(b) and (c) are issued under sec. 161(b), 68 Stat. 948, as amended 42 U.S.C. 2201(b); and §§35.14(b)(5)(ii), (iii) and (v) and (f)(2), 35.25 and 35.31(d) are issued under sec. 161o, 68 Stat. 950, as amended (42 U.S.C. 2201(o)).

* * *

2. In §35.14, paragraph (b)(7) is revised to read as follows:

§35.14 Specific licenses for certain groups of medical uses of by-product material.

* * * * *

(b)***

(7) The following radiopharmaceuticals, when used for the listed clinical procedures, are not subject to the restrictions in paragraph (b)(6) of this section:

(i) Technetium-99m pentetate as an aerosol for lung function studies;

(ii) Technetium-99m sulfur colloid as a solid or liquid for gastroesophageal imaging;

(iii) Technetium-99m sulfur colloid, pertechnetate, or macroaggregated human serum albumin for LeVeen shunt imaging;

(iv) Technetium-99m sulfur colloid, pertechnetate, or macroaggregated human serum albumin for ventriculo-atrial shunt imaging;

(v) Technetium-99m sulfur colloid, pertechnetate, or macroaggregated human serum albumin for ventriculo-peritoneal shunt imaging;

(vi) Technetium-99m pertechnetate for cystography; and

(vii) Technetium-99m pertechnetate for dacryocystography.

* * * * *

Dated at Bethesda, Maryland this _____ day of _____, 1984.

For the Nuclear Regulatory Commission

_____
William J. Dircks,
Executive Director for Operations.

DESIGNATOR AB72-1

Proposed Rules

Federal Register
Vol. 50, No. 77
Monday, April 22, 1985

PDR (EE)

This section of the FEDERAL REGISTER contains notices to the public of the proposed issuance of rules and regulations. The purpose of these notices is to give interested persons an opportunity to participate in the rule making prior to the adoption of the final rules.

NUCLEAR REGULATORY COMMISSION

10 CFR Part 35

Physician's Use of Radioactive Drugs

AGENCY: Nuclear Regulatory Commission.

ACTION: Proposed rule.

SUMMARY: The Nuclear Regulatory Commission (NRC) is proposing to amend its regulations to allow physicians to use technetium-99m labeled sulfur colloid for gastroesophageal imaging; technetium-99m labeled sulfur colloid, pertechnetate, and macroaggregated human serum albumin for LeVeen, ventriculo-atrial and ventriculo-peritoneal shunt imaging; and technetium-99m labeled pertechnetate for cystography and dacryocystography. Without this amendment, each NRC licensee that wants to use these radioactive materials in these ways would have to apply to the NRC for permission to do so. The proposed rule will allow physicians or hospitals that are now licensed by NRC to use other similar materials to use these drugs without making an application to NRC.

DATE: Comment period expires May 22, 1985.

Comments received after this date will be considered if it is practical to do so, but assurance of consideration cannot be given except as to comments received on or before this date.

ADDRESSES: Send comments to: The Secretary of the Commission, U.S. Nuclear Regulatory Commission, Washington, DC 20555, ATTN: Docketing and Service Branch. Hand deliver comments to: Room 1121, 1717 H Street NW., Washington, DC between 8:15 am and 5:00 p.m. Examine comments received, environmental and regulatory analyses and the requests for exception at: The NRC Public Document Room 1717 H Street, NW, Washington, DC.

FOR FURTHER INFORMATION CONTACT: Norman L. McElroy, Office of Nuclear Materials Safety and Safeguards, U.S. Nuclear Regulatory Commission, Washington, DC 20555, Telephone: (301) 427-4108.

SUPPLEMENTARY INFORMATION: Physicians who want to use certain readioactive materials in the practice of medicine may do so only in accordance with a license issued by the Nuclear Regulatory Commission (NRC) or by States which have an agreement with the NRC to license the use of these materials instead of the NRC.

As new radiopharmaceuticals, radioactive sources, medical devices, and uses of radioisotopes are developed, the NRC considers adding them to one of the groups under which medical licenses are issued. The groups were designed to allow physicians and community hospitals wide access to nuclear medicine services. The groups in § 35.100 contain only radiopharmaceuticals that are the subject of an FDA-approved "New Drug Application" (NDA), or a "Notice of Claimed Investigational Exemption for a New Drug" (IND) that has been accepted by FDA. A licensee authorized to use all the materials listed in a group is referred to as a "group medical licensee."

NRC regulations in § 35.14(b)(6) that apply to the group medical licensees provide that when a physician uses byproduct material for clinical procedures other than those approved by FDA and specified in the product labeling or package insert, the physician must follow the product labeling regarding: (1) Chemical and physical form, (2) route of administration, and (3) dosage range. The NRC has received requests to amend its regulations to allow physicians to use technetium-99m labeled sulfur colloid for gastroesophageal imaging; technetium-99m labeled sulfur colloid, pertechnetate, and macroaggregated human serum albumin for LeVeen, ventriculo-atrial, and ventriculo-peritoneal shunt imaging; and technetium-99m labeled pertechnetate for cystography and dacryocystography. These are clinical procedures that are not listed in the product labels.

(As a separate matter, the NRC recently allowed persons who are licensed to use materials in § 35.100 Group II or III to also use pertechnetate for dacryocystography and sulfur colloid for gastroesophageal imaging (see 50 FR 7663, published February 25, 1985). That action was precipitated by a letter to NRC from FDA that said those two methods of use had recently been approved for listing on the respective package inserts, but that some manufacturers might not be able to print new package inserts for several months. The NRC has included those two methods of use in this proposed rulemaking so that the regulation will provide a complete list.)

It is noteworthy that NRC and FDA have sought a solution to the general problem of drug labeling, and FDA currently is considering a program to authorize additional clinical procedures that use approved radiopharmaceuticals. However, until such a program is implemented, NRC believes that this rulemaking is the most appropriate way to resolve the problem in this interim period. This policy was described in an NRC rulemaking published in the Federal Register on February 3, 1983 (48 FR 5217).

The requests that NRC received provided a description of the clinical procedure, a justification for why the regulatory action is needed, the purpose of the procedure, an analysis of the radiation dose, and additional technical and scientific information. (Each of the requests is available for inspection at the NRC Public Document Room, 1717 H Street, NW, Washington, DC.) The NRC has reviewed the requests to determine whether the requested regulatory action might result in an unreasonable risk to the safety of the public or might endanger life or property. The NRC specifically considered two criteria:

- No unjustified dose to the patient, and
- Demonstration of adequacy of occupational radiation protection measures.

With assistance from its Advisory Committee on the Medical Uses of Isotopes (ACMUI), the NRC has determined that the above criteria have been met for the proposed clinical procedures. Many of the committee members believe that these clinical procedures are useful, and the risk/benefit ratio for these procedures is extremely low. They also noted that these techniques will probaby become routine when allowed by NRC.

Technetium-99m labeled sulfur colloid can be administered orally either as a solid or liquid test meal. Following oral administration, technetium-99m sulfur colloid goes from the esophagus to the stomach, small intestine, and the upper large intestine. This clinical procedure permits external imaging which is helpful in assessing gastric emptying, gastroesophageal reflux, and esophageal transit. The gastric emptying procedure is useful in demonstrating the presence and the severity of gastric motor disorder; the gastroesophageal reflux study may demonstrate backward flow in the digestive tract. The esophageal transit study may demonstrate obstructions or abnormal transit time. The normal dosage is 0.3 millcuries. The radiation dose to an average adult patient from 1 millicurie of orally administered technetium-99m sulfur colloid as a liquid is: 0.1 rad to the stomach wall; 0.3 rad to the small intestine; 0.5 rad to the upper large intestine; 0.3 rad to the lower large intestine; 0.1 rad to the ovaries; 0.01 rad to the testes; and 0.02 rad to the whole body. The estimated absorbed radiation dose to an average adult patient from 1 millicurie of orally administered technetium-99m sulfur colloid as a solid food is: 0.2 rad to the stomach wall; 0.2 rad to the small intestine; 0.4 rad to the upper large intestine; 0.3 rad to the lower large intestine; 0.1 rad to the ovaries, 0.004 rad to the tests; and 0.02 rad to the whole body.

These estimated absorbed radiation doses and the following doses are similar to other absorbed doses received from other diagnostic nuclear medicine and x-ray procedures.

A LeVeen shunt is an implanted tube that drains built-up fluid from the peritioneal cavity to a large central vein. Technetium-99m labeled sulfur colloid, pertechnetate, or macroaggregated human serum albumin can be injected into the peritoneal cavity to diagnose shunt malfunction, such as blockage by clot or valve failure, by taking images of the shunt. The normal dosage is 3 to 10 millicuries. The radiation dose from an intraperitoneal injection of a 3 millicurie dosage of technetium-99m sulfur colloid is: 0.02 rad to the whole body; 0.02 rad to the tests; 0.02 rad to the ovaries; 0.03 rad to the liver; 0.02 rad to the spleen and 0.03 rad to the red marrow.

A ventriculo-atrial shunt is a tube implanted in patients with hydrocephalus (fluid build-up in the head). It drains the fluid from the head to the atrial cavity. Technetium-99m labeled colloid, pertechnetate, or macroaggregated human serum albumin is injected into the shunt system of the patient to localize shunt blockage before surgical repair is performed. The normal dosage is 1 to 5 millicuries. The radiation dose from an injection of a 5 millicurie dosage of technetium-99m to a patient with a patent shunt is: 0.1 rad to the whole body and 0.1 rad to the brain.

A ventriculo-peritoneal shunt is an implanted tube in patients with hydrocephalus (fluid build-up in the head). It drains the fluid from the head to the peritoneal cavity. Technetium-99m labeled sulfur colloid, pertechnetate, or macroaggregated human serum albumin is injected into the shunt of patients to localize blockage before performing surgical repairs. The normal dosage is 1 to 5 millicuries. The radiation dose from an injection of a 5 millicurie dosage of technetium-99m to a patient with a patent shunt is: 0.1 rad to the whole body and 0.1 rad to the brain.

Cystography is a procedure for patients with bladder problems. A tube is inserted into the bladder of a patient. Technetium-99m pertechnetate is instilled through the tube into the bladder. Images are taken during filling and voiding of the bladder to measure the amount of reflux (backward flow) into the upper tracts, bladder volume at which reflux occurs, drainage time of reflux after voiding, and the remaining urine volume. The normal dosage is 1 millicurie. The radiation dose from a 1 millicurie dosage of technetium-99m pertechnetate is: 0.002 rad to the whole body, 0.006 rad to gonads, and 0.2 rad to the bladder.

Dacryocystography is a procedure for patients whose eyes exhibit excessive teardrops (epiphora). This procedure is performed to assess tear production and drainage in patients, and for nasolacrimal system imaging. Technetium-99m labeled pertechnetate is administered as a sterile eye drop. The normal dosage is 100 to 250 microcuries. The radiation dose from a dosage of 100 to 150 microcuries of technetium-99m pertechnetate per eye drop to the germinal epithelium of the lens is: 0.01 to 0.02 rad under normal physiological conditions. With blocked lacrimal drainage, the dose to the lens is 0.4 to 0.6 rad.

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 this is not a major Federal action significantly affecting the quality of the human environment and therefore an environmental impact statement is not required. The assessment shows that any detectable effect on the environment is unlikely. The environmental assessment and finding of no significant impact on which this determination is based are available for inspection at the NRC Public Document Room, 1717 H Street, NW, Washington, DC. Single copies of the environmental assessment are available from Mr. McElroy (*See* "**FOR FURTHER INFORMATION CONTACT**" heading).

Paperwork Reduction Act Statement

This proposed rule contains no information collection requirements and therefore it is not subject to the requirements of the Paperwork Reduction Act of 1980 (44 U.S.C. 3501 *et seq.*).

Regulatory Analysis

The NRC has prepared a draft regulatory analysis for this proposed rule. The analysis examines the costs and benefits of the alternatives considered by the NRC Public Document Room, 1717 H Street, NW, Washington, DC. A single copy may be obtained from Mr. McElroy (*See* "For Further Information Contact" heading).

Regulatory Flexibility Certification

As required by the Regulatory Flexibility Act of 1980, 5 U.S.C. 605(b), the NRC certifies that the rule, if adopted, will not have a significant economic impact on a substantial number of small entities. The NRC has prepared a draft regulatory analysis for this proposed rule that examines the economic impact of this action. The analysis notes that approximately 1900 medical licensees may experience some beneficial impact from the rule. The proposed rule would spare each medical licensee who desires to use the radioactive material in the requested manner the estimated $230 cost of preparing a license amendment request, the $120 amendment fee, and the 60-day delay associated with the amendment of the license.

The Commission is seeking comment particularly from small entities (*i.e.*, small businesses, small organizations, and small jurisdictions as defined by the Regulatory Flexibility Act) about the ways the proposed rule will affect them and the ways it may be modified to impose less stringent requirements on them which will still adequately protect the public health and safety. Those small entities that offer comments on how the regualtions could be modified to take it to account their differing needs should specifically discuss:

(a) The size of their business and how the proposed regulations would result in a significant economic burden upon them as compared to larger organizations in the same business community;

(b) How the proposed regulation could be modified to take into account their differing needs or capabilities;

(c) The benefits that would accure, or the detriments that would be avoided, if the proposed regulation were modified as suggested by the commenter;

(d) How the proposed regulation, as modified, would more closely equalize the impact of NRC regulations or create more equal access to the benefits of Federal programs as opposed to providing special advantages to any individuals or groups; and

(e) How the proposed regulation, as modified, would still adequately protect the public health and safety.

List of Subjects in 10 CFR Part 35

Byproduct material, Drugs, Health facilities, Health professions, Incorporation by reference, Medical devices, Nuclear materials, Occupational safety and health, Penalty, 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. 553, the following amendment to 10 CFR Part 35 is being considered.

PART 35—HUMAN USES OF BYPRODUCT MATERIAL

1. The authority citation for Part 35 continues 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); §§ 35.2, 35.14(b), (e) and (f), 35.21(a), 35.22(a), 35.24, and 35.31(b) and (c) are issued under sec. 161(b), 68 Stat. 948, as amended 42 U.S.C. 2201(b); and §§ 35.14(b)(5)(ii), (iii) and (v) and (f)(2), 35.25 and 35.31(d) are issued under sec. 161o, 68 Stat. 950, as amended (42 U.S.C. 2201(o)).

* * * * *

2. In § 35.14, paragraph (b)(7) is revised to read as follows:

§ 35.14 Specific licenses for certain groups of medical uses of byproduct material.

* * * * *

(b) * * *

(7) The following radiopharmaceuticals, when used for the listed clinical procedures, are not subject to the restrictions in paragraph (b)(6) of this section:

(i) Technetium-99m pentetate as an aerosol for lung function studies;

(ii) Technetium-99m sulfur colloid as a solid or liquid for gastroesophageal imaging;

(iii) Technetium-99m sulfur colloid, pertechnetate, or macroaggregated human serum albumin for LeVeen shunt imaging;

(iv) Technetium-99m sulfur colloid, pertechnatate, or macroaggregated human serum albumin for ventriculo-atrial shunt imaging;

(v) Technetium-99m sulfur colloid, pertechnetate, or macroaggregated human serum albumin for ventriculo-peritioneal shunt imaging;

(vi) Technetium-99m pertechnetate for cystography; and

(vii) Technetium-99m pertechnetate for dacryocystography.

* * * * *

Dated at Bethesda, Maryland this 5th day of April 1985.

For the Nuclear Regulatory Commission.

William J. Dircks,

Executive Director for Operations.

[FR Doc. 85-9853 Filed 4-19-85; 8:45 am]

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DEPARTMENT OF HOUSING AND URBAN DEVELOPMENT

Office of Assistant Secretary for Housing—Federal Housing Commissioner

24 CFR Parts 207 and 213

[Docket No. R-85-1106; FR-1758]

Cooperative Housing Mortgage Insurance—Subordinated Secretary-Held Mortgages

AGENCY: Office of the Assistant Secretary for Housing—Federal Housing Commissioner, HUD.

ACTION: Proposed rule.

SUMMARY: This proposed rule would, under stated conditions, permit unsubsidized multifamily rental housing projects with Secretary-held mortgages to be converted to cooperatives by subordinating the Secretary-held mortgage to a new first mortgage insured under section 213(i) of the National Housing Act.

This proposal is expected to benefit both the tenants of an affected project and the General Insurance Fund. Tenants would gain the opportunity for cooperative homeownership at a lower cost, since the interest on the Secretary-held mortgage would remain at its original rate. The General Insurance Fund would benefit by sharing in fifty percent of the equity appreciation received by the project owner in selling the project to a cooperative.

DATE: Comments due: June 21, 1985.

ADDRESS: Interested persons are invited to submit comments about this rule to the Office of the General Counsel, Rules Docket Clerk, Room 10276, Department of Housing and Urban Development, 451 Seventh Street, SW., Washington, D.C. 20410. Letters should refer to the above docket number and title. A copy of each comment received will be available for public inspection and copying (at a charge of 10 cents per page) during regular business hours at the above address.

FOR FURTHER INFORMATION CONTACT: James L. Hamernick, Director, Office of Housing, Multifamily Housing Development, Room 6128, Department of Housing and Urban Development, 451 Seventh Street, S.W., Washington, D.C. 20410, (202) 755-5720. (This is not a toll-free number.)

SUPPLEMENTARY INFORMATION: With the exception of certain supplementary loans under section 213(j), 232(i) or 241 of the National Housing Act (Act), or operating loss loans under section 223(d) of the Act, HUD is not authorized to insure a project mortgage which has been subordinated to any other first lien. The Act, however, does not prohibit HUD from allowing an already-existing first mortgage to be subordinated, after HUD has become the mortgagee. By amending 24 CFR 213.21 and 213.22, and by making conforming amendments to §§ 213.7, 207.253a, and 207.258, this proposed rule would allow an unsubsidized multifamily rental housing project with a Secretary-held mortgage to be converted to a cooperative by subordinating the existing Secretary-held mortgage to a new National Housing Act section 213(i) insured first mortgage.

The new section 213(i) insured first mortgage would be for an amount no greater than the difference between (a) the maximum insured mortgage which would be available under Section 213(i) if the project were being refinanced, and (b) the unpaid principal obligation of the existing Secretary-held mortgage. In order to protect the interests of the government as a secondary lienholder, and to enable a certain amount of the insurance proceeds that was paid to the mortgagee to be recouped upon the conversion, provisions are proposed to be added to the regulations to enable HUD to share in the equity appreciation realized by the mortgage in selling the property to a cooperative, and to require