JAN 17 1985

UNITED STATES
NUCLEAR REGULATORY COMMISSION
WASHINGTON, D. C. 20555

~~Kathy~~
Harry

JAN 14 1985

MEMORANDUM FOR: Frank P. Gillespie, Chairman
RES Independent Review Board

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

SUBJECT: ADDENDUM TO RES INDEPENDENT REVIEW OF PROPOSED RULEMAKING

This is an addendum to our December 26, 1984 review package concerning NMSS's modification of 10 CFR 35.14(b)(7) to add six new methods of use and the appropriate radiopharmaceuticals for each. It should be noted that NMSS based its decision to include these new medical procedures on the criteria given in the February 28, 1983 Federal Register Notice entitled, "Physician's Use of Radioactive Drugs." These two criteria are:

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

In addition to the staff evaluation, members of NRC's Advisory Committee on the Medical Uses of Isotopes were consulted for their recommendations. For the particular uses to be included, the health and safety considerations for the additional uses are no greater than for the uses specified in the respective package labels. These considerations were implicit in the review, but we decided they should be transmitted in writing.

Karl R Goller

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

MEMORANDUM FOR: William J. Dircks
Executive Director for Operations

FROM: Robert B. Minogue, Director
Office of Nuclear Regulatory Research

SUBJECT: CONTROL OF NRC RULEMAKING: RES INDEPENDENT REVIEW OF PROPOSED RULEMAKING SPONSORED BY NMSS

Based on our independent review of the proposed rulemaking sponsored by NMSS to modify §35.14(b)(7) of 10 CFR Part 35, "Human Uses of Byproduct Material," to add six new methods of use and the appropriate radiopharmaceuticals, RES agrees with the recommendation of the Director, NMSS, that this rulemaking effort should continue.

The basis for our recommendation is that this rulemaking concerns the specific implementation of NRC's policy for licensing radiopharmaceuticals that was described in the Federal Register on February 3, 1983. As such, it is a minor updating of the medical licensing groups.

The complete RES independent review package has been sent to OEDO (Attention: DEDROGR) and to the Director, NMSS.

Robert B. Minogue, Director
Office of Nuclear Regulatory Research

Enclosure:
As stated

DISTRIBUTION:

Subj. (C.4.1)	WAMills
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DRAFT STAFF RECOMMENDATION

Based on the staff review, DRPES finds that the proposed rulemaking should continue.

RESULTS OF RES STAFF REVIEW

a) The issue to be addressed.

This proposed rulemaking will add the following Food and Drug Administration (FDA) - approved drugs for the following new methods of use to §35.14(b)(7):

- technetium-99m labeled sulfur colloid for gastroesophageal imaging

- technetium-99m labeled sulfur colloid, pertechnetate, or macroaggregated human serum albumin for Le Veen, ventriculo-atrial, and ventriculo-peritoneal shunt imaging

- technetium-99m labled pertechnetate for cystography and dacryocystography.

As such, it is a specific implementation of NRC's policy for licensing radiopharmaceuticals as described in the Federal Register on February 3, 1983 (48 FR 5217). The purpose of the policy change was to allow presently licensed physicians or hospitals to use certain radiopharmaceuticals for recently developed methods of use not listed on their respective package labels.

b) The necessity and urgency for addressing the issue.

A large number of physicians have been waiting for FDA to issue a list of new approved uses for already approved radiopharmaceuticals. It now appears FDA will not take this step, but rather continue to follow the established procedure of waiting for the manufacturers to request a label change. Because of the costs involved relative to the additional sales, the manufacturers have no incentive to do this.

These new methods of use are not only better than older ones, they may even result in lower patient doses. In some cases, there is no other imaging method available.

c) Alternatives to rulemaking.

The only alternative is to amend individual licenses to authorize the new methods of use.

d) How the issue will be addressed through rulemaking.

The proposed rule would modify 10 CFR 35.14(b)(7) to add six new methods of use and the appropriate radiopharmaceuticals for each.

e) How the public, industry, and NRC will be affected.

Both the NRC and the licensees will benefit by eliminating costly and

time consuming license amendments. The patients will benefit from improved diagnostic methods.

f) NRC resources and scheduling.

NMSS estimates it will need about 0.1 staff-year to complete the proposed and final rulemaking. This seems reasonable.

List of Subjects in 7 CFR Part 910

Marketing agreements and orders, California, Arizona, Lemons.

PART 910—[AMENDED]

1. Section 910.697 is added as follows:

§ 910.697 Lemon Regulation 397.

The quantity of lemons grown in California and Arizona which may be handled during the period February 6, 1983 through February 12, 1983, is established at 210,000 cartons.

2. Section 910.696 Lemon Regulation 396 (48 FR 3935) is revised to read as follows:

§ 910.696 Lemon Regulation 396.

The quantity of lemons grown in California and Arizona which may be handled during the period January 30, 1983, through February 5, 1983, is established at 200,000 cartons.

(Secs. 1–19, 48 Stat. 31, as amended; 7 U.S.C. 601–674).

Dated: February 3, 1983.

D. S. Kuryloski,

Deputy Director, Fruit and Vegetable Division, Agricultural Marketing Service.

[FR Doc. 83-3267 Filed 2-3-83; 11:58 am]

BILLING CODE 3410-02-M

NUCLEAR REGULATORY COMMISSION

10 CFR Part 35

Physician's Use of Radioactive Drugs

AGENCY: Nuclear Regulatory Commission.

ACTION: Final rule.

SUMMARY: The Nuclear Regulatory Commission (NRC) is amending its regulations to provide an exception from certain regulatory requirements for technetium-99m pentetate (a Food and Drug Administration (FDA)-approved drug) used for lung function studies which is a use not yet approved by FDA. Prior to this final rule, NRC regulations required that a physician using an approved drug for an unapproved procedure follow FDA-approved labeling for (1) physical form, (2) route of administration, and (3) dosage range. Because in the lung function studies, technetium-99m pentetate is used as an aerosol and administered by inhalation, it does not meet the FDA-approved method for use of this radiopharmaceutical, and an exception is necessary. The preamble to this rulemaking also sets out the criteria and procedures that NRC will use to evaluate similar requests for exceptions of other diagnostic radiopharmaceuticals. This final rule responds to the petition filed by the late Dr. George V. Taplin to approve the use of technetium-99m pentetate for lung function studies (PRM 35–1). The final rule will relieve many of NRC's medical licensees from applicable regulatory requirements. The final rule and the new exception procedures are intended to remove unnecessary restrictions on the physician in patient treatment while continuing to provide an adequate level of radiation protection for the patient and the worker.

EFFECTIVE DATE: March 7, 1983.

FOR FURTHER INFORMATION CONTACT: Deborah A. Bozik, Office of Nuclear Regulatory Research, U.S. Nuclear Regulatory Commission, Washington, DC, 20555 (Phone 301–427–4566).

SUPPLEMENTARY INFORMATION: On April 13, 1982, the NRC published a proposed rule (47 FR 15798) to amend its regulations to provide an exception from certain regulatory requirements for technetium-99m pentetate in § 35.14 of 10 CFR Part 35, which contains the specific license requirements for certain groups of medical uses of byproduct material. In addition, this proposed rule also offered criteria and information for evaluation of similar future exceptions to NRC regulations.

This rulemaking was developed in response to a petition filed by George V. Taplin, M.D. (deceased) for a rulemaking to remove NRC restrictions that apply when a physician uses an FDA-approved radioactive drug for a clinical procedure that does not have FDA approval. Specifically, the petitioner sought the nonrestricted use of technetium pentetate as an aerosol for lung function studies (PRM–35–1; 44 FR 26817; May 1, 1979). The NRC grants that portion of the petition that requests a specific exception for technetium-99m pentetate used for lung function studies. The NRC denies the petitioner's request that NRC remove all restrictions on the physican's use of an FDA-approved radioactive drug for a clinical procedure that does not have FDA approval. However, the procedures and criteria established in this rulemaking create an appropriate mechanism for addressing future requests for exceptions to these restrictions and, as such, are an attempt to provide the greater flexibility desired by the petitioner.

The public was invited to submit written comments on the proposed rule by June 14, 1982, and 35 comment letters were received. Thirty-one commenters supported the proposed rule, and 15 specifically noted their support of the criteria and procedures for evaluating similar future exceptions. Copies of the public comments received and the Commission analysis of the comments may be examined in the Commission's Public Document Room at 1717 H Street, N.W., Washington, D.C.

Two commenters opposed the proposed rule because of their feeling that NRC would be authorizing the addition of non-FDA-approved procedures to its regulations, thereby starting a precedent for such procedures to be added without close evaluation. Careful consideration was given to the questions raised by these commenters, but the NRC does not believe that patient protection is being compromised. Technetium-99m penetetate gives several times less radiation to the lung than other radiopharmaceuticals which are more slowly absorbed and thus are retained longer in the lungs. Taplin and Chopra, "Inhalation Lung Imaging with Radioactive Aerosols and Gases," Prog. Nucl. Med., Vol. 5, pp. 119–143 (Karger, Basel 1978), and Taplin and Chopra, "Lung Perfusion-Inhalation, Scintigraphy in Obstructive Airway Disease and Pulmonary Embolism," Radiological Clinics of North America, Vol. XVI, No. 3, pp. 491–513, December 1978.

It is noteworthy that NRC and FDA have sought a solution to the general problem of drug labeling for unapproved uses, and FDA currently is considering a program to add presently unapproved uses of 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. Nine commenters either addressed topics not specifically covered in this rulemaking or requested that NRC consider other unapproved uses of FDA-approved radiopharmaceuticals. The most common requests centered on the uses of technetium-99m pertechnetate for voiding cystograms and technetium-99m sulfur colloid for evaluation of LeeVeen shunt patency. NRC developed criteria and procedures for evaluating exceptions to § 35.14(b)(6). These procedures and criteria were published in the April 13, 1982 proposed rule and were open to the public for comment. They were very favorably received. The Commission will use these criteria to determine whether an exception from the requirements in § 35.14(b)(6) of 10 CFR Part 35 will result in an unreasonable risk to the health and safety of the public or will minimize danger to life or property.

Any interested person should submit a request for an exception to NRC's Office of Nuclear Material Safety and

Safeguards detailing the following information:

- Description of the procedures,
- Justification for the exception (including an explanation of why the procedure is not included in the product labelling),
- Purpose and benefits of the procedure,
- Analysis of the radiation dose, and
- Supporting technical and scientific information, including any provisions necessary to ensure occupational safety and patient safety.

In order to reach a conclusion regarding the possible inclusion of these radiopharmaceuticals in the regulations, NRC would expect that such requests would provide evidence that the following two criteria, upon which NRC will conduct its assessment, would be met:

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

The NRC staff would review a request, and based upon its findings as well as the recommendation of its Advisory Committee on the Medical Uses of Isotopes (ACMUI), would publish in the **Federal Register** a notice of rulemaking. The notice would provide for a 30- to 45-day comment period. The final rule establishing the exception would be made immediately effective.

Environmental Impact: Negative Declaration

The Commission has determined under the National Environmental Policy Act of 1969, as amended, and the Commission's regulations in 10 CFR Part 51, that promulgation of this regulation is not a major Federal action significantly affecting the quality of the human environment and therefore an environmental impact statement is not required. The environmental impact appraisal and negative declaration on which this determination is based are available for public inspection at the NRC Public Document Room, 1717 H St. NW., Washington, D.C.

Paperwork Reduction Act Statement

Pursuant to the provisions of the Paperwork Reduction Act of 1980 (44 U.S.C. 3501, et seq.), the NRC has made a determination that this rule would not impose new recordkeeping, application, reporting, or other types of information collection requirements.

Regulatory Flexibility Certification

In accordance with the Regulatory Flexibility Act of 1980, 5 U.S.C. 605(b), the Commission hereby certifies that this rule will not have a significant economic impact upon a substantial number of small entities. The final rule affects about 2,000 specific licenses under §§ 35.11, 35.12, and 35.14 of 10 CFR Part 35. These licenses are issued principally to medical institutions. Small business entities, primarily physicians in private practice, comprise about 275 of the specific medical licenses.

The final rule relieves NRC's medical licensees from regulatory requirements by relaxing restrictions on the physician concerning patient care. The final rule has no significant economic impact on these licensees. In the proposed rule, the NRC specifically requested comments on this conclusion as to impact on small entities. No comments were received that questioned this conclusion.

List of Subjects in 10 CFR Part 35

Byproduct material, Drugs, Health facilities, Health professions, Medical devices, Nuclear materials, Occupational safety and health, Penalty, Radiation protection, Reporting and recordkeeping requirements.

Under the Atomic Energy Act of 1954, as amended, the Energy Reorganization Act of 1974, as amended, and section 553 of Title 5 of the United States Code, the following amendments to Title 10, Chapter I, Code of Federal Regulations, Part 35, are published as a document subject to codification.

PART 35—HUMAN USES OF BYPRODUCT MATERIAL

1. The authority citation of 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. 161b, 68 Stat. 948, as amended (42 U.S.C. 2201(b)); and §§ 35.14(b)(5) (ii), (iii), and (v) and (f)(2), 35.27 and 35.31(d) are issued under sec. 161o, 68 Stat. 950 as amended (42 U.S.C. 2201(o)).

2. Section 35.14 is amended by revising paragraph (b)(6) and adding paragraphs (b)(7) and (b)(8) to read as follows:

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

* * * * *

(b) * * *

(6) Except for those radiopharmaceuticals listed in paragraph (b)(7) of this section, for Groups I, II, and III any licensee using byproduct material for clinical procedures other than those specified in the product labeling (package insert) shall comply with the product labeling regarding:

(i) Chemical and physical form;

(ii) Route of administration; and

(iii) Dosage range.

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

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

(8) Radioactive aerosols must be administered with a closed, shielded system that either is vented to the outside atmosphere through an air exhaust or provides for collection and disposal of the aerosol.

* * * * *

Dated at Bethesda, MD, this 28th day of January, 1983.

For the Nuclear Regulatory Commission.

William J. Dircks,

Executive Director for Operations.

[FR Doc. 83-3221 Filed 2-3-83; 8:45 am]

BILLING CODE 7590-01-M

DEPARTMENT OF ENERGY

10 CFR Part 810

Unclassified Activities in Foreign Atomic Energy Programs

AGENCY: Energy.

ACTION: Final rule.

SUMMARY: Pursuant to the Nuclear Non-Proliferation Act of 1978 (NNPA) and in accordance with the Executive Branch Procedures established and published June 9, 1978 (43 FR 25326), the Department of Energy (DOE) is amending its regulations, 10 CFR Part 810 "Unclassified Activities in Foreign Atomic Energy Programs." The amended regulations reflect changes made by the NNPA to Section 57.b. of the Atomic Energy Act and incorporate the additional export criteria mandated by the NNPA to govern the export of sensitive nuclear technology for peaceful purposes. The amended regulations update the list of countries to which the general authorization contained in § 810.7(a) does not apply. Added to the listed countries are all non-nuclear weapon states that are not parties to the Treaty on the Non-Proliferation of Nuclear Weapons (NPT) (except for those that accept fullscope safeguards or for which the Treaty of Tlatelolco is currently in force) and certain countries in regions of particular volatility and sensitivity. Withdrawal of the general authorization to these countries will assure that authorizations

OFFICE REVIEW PACKAGE RECEIVED FROM NMSS

* U. S. GOVERNMENT PRINTING OFFICE: 1981—335-960

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EDO	12-7-84	12-11-84	RES-84-2721

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ACTION NECESSARY	NO ACTION NECESSARY	CONCURRENCE	COMMENT	DATE ANSWERED:	BY:
XX	☐	☐	☐		

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DESCRIPTION: (Must Be Unclassified)

MEMO FM. J. DAVIS,NMSS,TO DIRCKS DTD 12/7/84--SUBJ: RECOMMENDATION TO INITIATE MINOR RULEMAKING

ENCLOSURES:

1. DIRCKS REGULATORY AGENDA ENTRY
2. DRAFT REGULATORY ANALYSIS

REMARKS:

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INFOCY:MINOGUE			
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U. S. NUCLEAR REGULATORY COMMISSION

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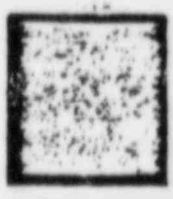

MEMORANDUM FOR: Williams J. Dircks
Executive Director for Operations

THRU: James J. Henry, Coordinator
Research Independent Review Board

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

SUBJECT: RECOMMENDATION TO INITIATE MINOR RULEMAKING

The following information is submitted in response to your directive of May 30, 1984 that the office sponsoring a rulemaking assemble a rulemaking review package.

1. This rulemaking will allow NRC licensees to use Food and Drug Administration (FDA) approved radiopharmaceuticals for some recently developed methods of use that are not listed on the respective package labels. This implements NRC policy (48 FR 5217, February 4, 1983).

2. Although not urgent, this will facilitate potentially beneficial new uses of approved drugs.

3. The only alternative to the rulemaking would be to amend individual licenses to authorize the new methods of use; that would consume an inordinate amount of staff time.

4. The proposed rule would modify 10 CFR 35.14(b)(7) to add six new methods of use and the appropriate radiopharmaceuticals for each.

5. The proposed rule would make the new diagnostic methods of use available to NRC licensees and their patients. There is no increase in cost or worker dose for licensees. This is the most efficient way for NRC to authorize the new methods of use.

6. NRC would need about 0.1 staff year to complete the proposed rulemaking and final rulemaking. The proposed rule can be published in January 1985 and the final rule in April 1985.

OFFICE ▶							
SURNAME ▶							
DATE ▶							

I recommend that the office proceed with this proposed rulemaking.

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

Enclosures:
1. Draft Regulatory Agenda Entry
2. Draft Regulatory Analysis

cc: John Clarke
Cost Analysis Group

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SURNAME	NLMcElroy/pj	VLMiller	DRChapell	RECunningham	DMausshardt	JGDavis	JJHenry
DATE	11/28/84	11/28/84	12/3/84	12/3/84	12/4/84	11/ /84	11/ /84

NRC FORM 318 (10-80) NRCM 0240 OFFICIAL RECORD COPY

DRAFT REGULATORY AGENDA ENTRY

ABSTRACT

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. Although not urgent, this will facilitate potentially beneficial new uses of approved drugs. The only alternative to the rulemaking would be to amend individual licenses to authorize these new methods of use; that would consume an inordinate amount of staff time. The proposed rule would allow NRC-licensed physicians to use some currently available diagnostic radiopharmaceuticals for some recently developed methods of use that are not listed on the respective package labels. NRC will use about 0.1 staff-year to complete the proposed rulemaking and final rulemaking.

DEC 17 1984

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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.

DEC 11 1984

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:

- o No unjustified radiation dose to the patient, and
- o 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.

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

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 Chapter 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

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.

DEC 11 1984

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.

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 Section 35.14(b)(7) of 10 CFR 35 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 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 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 unnecesary 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 ACMUI, will analyze the public comments received and prepare a final rule. The Material Licensing Branch will mail copies of the proposed and final rule to affected licensees.

Designator "AB72-1" PDR EE

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 may also use radiopharmaceuticals for the new methods of use listed in §35.14(b)(7) of 10 CFR Part 35, "Human Uses of Byproduct Material." 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 radiopharmaceuticals 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: List the new methods of use in §35.14(b)(7). Affected licensees would be able to use the radiopharmaceuticals for the new 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.

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

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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 a 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.

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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 the filling and voiding of the bladder to measure the actual amount of reflux (backward flow) into the upper tracts, to quantitate the bladder volume at which reflux occurs, to calculate the 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 allow physicians to use the new method of use rather than imposing its usual requirement that they 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, allow physicians to use the approved radiopharmaceuticals for the new methods of use.

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

Impact:

Without this rulemaking, a licensee authorized to use these radiopharmaceuticals for approved uses could not use them for the new methods of use 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.