AE23-2
PDR

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

SEP 11 1992

MEMORANDUM FOR: C. J. Heltemes, Jr., Deputy Director for Generic Issues and Rulemaking
Office of Nuclear Regulatory Research

FROM: Patricia G. Norry, Director
Office of Administration

SUBJECT: OFFICE CONCURRENCE ON FINAL RULE ENTITLED, "DEPARTURES FROM MANUFACTURER'S INSTRUCTIONS; ELIMINATION OF RECORDKEEPING REQUIREMENTS"

The Office of Administration concurs on the final rule entitled "Departures From Manufacturer's Instructions; Elimination of recordkeeping Requirements." We have attached a marked copy of the final rule that presents a number of editorial comments and format corrections.

Please note that when the final rule is forwarded to the Executive Director for Operations (EDO), it should be presented under a memorandum to the EDO that requests his signature and approval. The package should contain an "Approved for Publication" sheet and an entry for insertion in the Daily Staff Notes (see section 15.4 of the NRC Regulations Handbook).

We have forwarded a copy of the final rule to the Information and Records Management Branch, IRM for their comment or concurrence concerning the paperwork management aspects of this rulemaking action. We have requested that they respond directly to you.

In order to assist you in preparing the list of documents centrally relevant to this final rule that is required by NRC's regulatory history procedures, you should place the designator "AE23-2" in the upper right-hand corner of each document concerning the rule that you forward to the Nuclear Document System.

If you have any questions concerning this matter, please have a member of your staff contact Michael T. Lesar (27758).

Patricia G. Norry, Director
Office of Administration

Attachment: As stated

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[7590-01]

NUCLEAR REGULATORY COMMISSION

10 CFR Parts 30 and 35

RIN: 3150 - AE23

Departures From Manufacturer's Instructions;

Elimination of Recordkeeping Requirements

AGENCY: Nuclear Regulatory Commission.

ACTION: Final rule.

SUMMARY: The Nuclear Regulatory Commission (NRC) is amending its regulations to eliminate certain recordkeeping requirements related to the preparation and use of radiopharmaceuticals. Specifically, this rule eliminates recordkeeping requirements related to the justification for and a precise description of the departure, and the number of departures from the Food and Drug Administration (FDA) approved manufacturer's instructions. Both the NRC and the FDA staffs agree that the major trends in departures that may be identified by this recordkeeping are already discernible and collecting additional data is unnecessary.

EFFECTIVE DATE: [Insert date of publication.]

FOR FURTHER INFORMATION CONTACT: Samuel Z. Jones, Office of Nuclear Regulatory Research, U.S. Nuclear Regulatory Commission, Washington, DC 20555, telephone (301) 492-3738.

SUPPLEMENTARY INFORMATION:

Background

On September 15, 1989 (54 FR 38239), the NRC published in the Federal Register a notice of receipt of a petition for rulemaking (PRM-35-9) from the American College of Nuclear Physicians (ACNP) and the Society of Nuclear Medicine (SNM). The ACNP and SNM requested, among other things, that the NRC amend its regulations in 10 CFR Part 35, "Medical Use of Byproduct Material," to recognize their appropriate practice of medicine and to allow (1) departures from the manufacturer's instructions for preparing diagnostic radiopharmaceuticals and (2) the use of radiopharmaceuticals for therapeutic indications and methods of administration not included in the FDA approved package insert.

On August 23, 1990 (55 FR 34513), the NRC published in the Federal Register an Interim Final Rule granting the petition, in part, to specifically allow departures from the manufacturer's instructions for preparing diagnostic radiopharmaceuticals using generators and reagent kits for which the FDA has approved a New Drug Application (NDA). The Interim Final Rule also included recordkeeping requirements for the specific nature of the departure, a brief statement of the reasons for the departure, and the number of departures. The Interim Final Rule is effective through August 23, 1993. This action was taken after consulting with the FDA and with the intention that the provision might become permanent after further experience had been gained under the new provision, including an assessment of licensee documentation of departures. The NRC's original intent was to examine this documentation and make it

available to the FDA and to consult with the FDA prior to any decision regarding either revision or continuation of the Interim Final Rule or making it permanent. The NRC staff has recently consulted with the FDA staff on the documentation collected to date.

Based on this documentation, the NRC and FDA staffs concluded that the major trends in departures are already clear and that collecting additional data would not be expected to reveal any significant new information. On June 11, 1992, the NRC published in the Federal Register a proposed rule (57 FR 24763) ~~to~~ that suggested amendments to 10 CFR Parts 30 and 35 to eliminate recordkeeping requirements involving the justification for and a precise description of the departure, and the number of departures from the FDA approved manufacturer's instructions. The FDA staff had no objection to eliminating these recordkeeping requirements. The issue of whether departures, as set out in the Interim Final Rule, should be allowed on a permanent basis is currently under consideration by the NRC as part of its ~~on-going~~ effort to resolve PRM-35-9.

Public Comments and NRC's Responses

The NRC received nine comment letters in response to the proposed rule. In terms of the types of organizations, there were three comment letters from hospitals and clinics, two from professional associations, and one each from an Agreement State, a pharmacy, a Federal agency, and an individual member of the public. Eight of the letters supported the proposed amendments and one letter opposed the rule.

Brief descriptions of the issues raised in public comment letters and NRC's responses to those issues are presented ~~below~~ in the following paragraphs.

1. Comment: A commenter suggested that the NRC allow the disposition of records of departures generated under the Interim Final Rule after 3 years (instead of 5 years as specified in the Interim Final Rule) because the records have apparently served their purpose.

Response: The NRC agrees that the records have served their purpose and additional retention of these records is not necessary. This rule eliminates the retention period ~~of~~ for these records. Thus, as of the effective date of this rule, licensees are no longer required to keep records of departures carried out under the Interim Final Rule.

2. Comment: A commenter suggested the termination of the remainder of the Interim Final Rule in favor of the provisions detailed in the ACNP-SNM Petition (PRM-35-9) ~~of June 1988~~.

Response: The NRC is currently considering all issues raised in the ACNP-SNM Petition, including (NRC consideration) the continuation of departures as set out in the Interim Final Rule.

3. Comment: A commenter noted a typographical error in the text of ~~Section~~ § 35.200 of the proposed rule which indicated paragraph (i) instead of paragraph (c).

Response: This typographical error has been corrected.

4. Comment: A commenter suggested that if there are no public health and safety issues identified, the authorization to deviate should not expire on August 23, 1993.

Response: The purpose of this rule is to provide relief to licensees concerning the recordkeeping burden related to the requirements in the Interim

Final Rule. Therefore, the effective period of this rule was intentionally used to be consistent with the effective period of the Interim Final Rule.

The NRC anticipates that the ACNP-SNM petition (PRM-35-9), including the issues associated with the Interim Final Rule, will be resolved prior to August 23, 1993.

5. Comment. A commenter opposed this rule. The commenter provided the following rationale: (1) while reduction of regulatory burden may be a worthy goal, the legislative mandate to protect public health and safety must take precedence over an administrative goal; (2) the modification in this rule would invite and promote an attitude or climate which resulted in the Three Mile Island accident, and thus, would present a danger to the health and safety of the public; and (3) the NRC's rationale for this rule contradicts a statement made by the NRC, in a Federal Register notice announcing a public workshop (57 FR 27711; June 22, 1992), that some medical use licensees have administered byproduct material to patients who are pregnant or breast-feeding without knowing the patient's pregnancy or breast-feeding status.

Response. With respect to the first point, the elimination of the recordkeeping requirements addressed in this rule will not compromise public health and safety because this rule specifies that departures may only be made by following the directions of an authorized ~~user~~ physician. Therefore, NRC will continue to meet its legislative mandate. With respect to the second point, ~~since~~ licensees must continue to comply with all applicable regulatory requirements and will continue to be subject to the same inspection and enforcement efforts. Therefore, the NRC believes that licensees' attitudes will not be negatively affected by this rule, and thus will not present a danger to the health and safety of the public.

Concerning the statement made in the public workshop notice as related to the rationale for this rule, the NRC views these two regulatory issues as separate matters. The rationale for this rule is to eliminate a regulatory burden that is no longer needed. The NRC has collected data specific to licensees' departures from manufacturer's instructions. The NRC and FDA staffs have concluded that the major trends in departures are already clear and that collecting additional data would not be expected to reveal any significantly new information. This rule is not connected to the issue concerning inadvertent radiation exposures to an embryo, fetus, or breast-feeding infant. In particular, the NRC has not stated that departures from manufacturer's instructions have led to an unintended radiation exposure to an embryo, fetus, or breast-feeding infant. Also, the NRC staff is not aware of any cases involving an unintended radiation exposure to an embryo, fetus, or breast-feeding infant that has been caused by a licensee departing from a manufacturer's instructions. Therefore, the NRC sees no contradiction between the rationale for this rule and the statement made in the public workshop notice.

The issue regarding unintended radiation exposures to an embryo, fetus, or breast-feeding infant from medical use of byproduct material is currently under study by the NRC to determine whether any regulatory action is necessary.

Discussion of the Final Rule Text

Based on public comments and NRC's responses discussed above, no substantive changes to the final rule are necessary. Thus, the text of the

final rule remains the same as the proposed rule ~~text~~ with the exception that a typographical error in the proposed rule, paragraph (i) in ~~Section~~ 35.200, has been ~~relabeled~~ as paragraph (c) ~~in the final rule.~~

Environmental Impact: Categorical Exclusion

The NRC has determined that this final regulation is the type of action described in categorical exclusion 10 CFR 51.22 (c)(3)(ii). Therefore, neither an environmental impact statement nor an environmental assessment has been prepared for this final rule.

Paperwork Reduction Act

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

The public reporting burden for this collection of information is estimated to be reduced by .05 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, to the Information and Records Management Branch (MNBB-7714), U.S. Nuclear Regulatory Commission, Washirgton, DC 20555; and to the Desk Officer, Office of Information and Regulatory Affairs, NEOB-

3019, (3150-0010 and 3150-0017), Office of Management and Budget, Washington, DC 20503.

Regulatory Analysis

In August 1990, the NRC implemented an Interim Final Rule allowing licensees to depart from the manufacturer's instructions for preparing diagnostic radiopharmaceuticals, and to depart from the package insert instructions regarding use of radiopharmaceuticals for therapy, provided that certain conditions were met. One of the conditions was for licensees to maintain records of such departures.

On June 11, 1992, the NRC published in the Federal Register a proposed rule that would delete these recordkeeping requirements (57 FR 24763). Nine comment letters were received, eight supported and one opposed this rule.

The only alternative to this action is to continue to keep these records. However, the NRC and FDA staffs have concluded that the major trends in departures are already clear and that collecting additional data would not be expected to reveal any significant new information. Therefore, the NRC believes that these recordkeeping requirements are no longer necessary.

The estimated reduction in annual burden would be approximately 1000 hours for NRC licensees. The NRC concludes that this action is justified due to the net annual savings to NRC licensees and because eliminating these recordkeeping requirements would not affect public health and safety.

Regulatory Flexibility Certification

As required by the Regulatory Flexibility Act of 1980, 5 U.S.C. 605(b), the Commission certifies that this rule will not have a significant economic impact on a substantial number of small entities. This rule would affect medical use licensees including some private practice physicians. Some of these licensees would be considered small entities under the NRC's size standards (56 FR 56672; November 6, 1991). This rule eliminates recordkeeping requirements that the NRC and FDA staffs agree are no longer necessary. This action will reduce the regulatory burden on medical use licensees, including some small entities.

Backfit Analysis

The NRC has determined that the backfit rule, 10 CFR 50.109, does not apply to this rule, and therefore, a backfit analysis is not required for this rule, because these amendments do not involve any provisions which would impose backfits as defined in 10 CFR 50.109(a)(1).

List of Subjects

Part 30 - Byproduct material, Criminal penalty, Government contracts, Intergovernmental relations, Isotopes, Nuclear materials, Radiation protection, Reporting and recordkeeping requirements.

Part 35 - Byproduct material, Criminal penalty, Drugs, Health facilities, Health professions, Incorporation by reference, Medical devices, Nuclear materials, Occupational safety and health, Radiation protection, Reporting and recordkeeping requirements.

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

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

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

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

Section 30.7 also issued under Pub. L. 95-601, sec. 10, 92 Stat. 2951 (42 U.S.C. 5851). Section 30.34(b) also issued under sec. 184, 68 Stat. 954, as amended (42 U.S.C. 2234). Section 30.61 also issued under sec. 187, 68 Stat. 955 (42 U.S.C. 2237).

For the purposes of sec. 223, 68 Stat. 958, as amended (42 U.S.C. 2273); §§ 30.3, 30.10, 30.34(b), (c), (f), (g) and (i), 30.41 (a) and (c), and 30.53 are issued under sec. 161b, 68 Stat. 948, as amended (42 U.S.C. 2201(b)); §30.10 is issued under sec. 161i, 68 Stat. 949, as amended (42 U.S.C. 2201(i)); and §§ 30.6, 30.9, 30.34(g), 30.36, 30.50 30.51, 30.52, 30.55, and 30.56(b) and (c) are issued under sec. 161o, 68 Stat. 950, as

amended (42 U.S.C. 2201(o)).

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

§ 30.34 Terms and conditions of licenses.

* * * * *

(i)(1) From August 23, 1990, to August 23, 1993, each licensee eluting generators and processing radioactive material with diagnostic reagent kits for which the Food and Drug Administration (FDA) has approved a "New Drug Application" (NDA), may depart from the manufacturer's elution and preparation instructions (for radiopharmaceuticals authorized for use pursuant to 10 CFR 35.200), provided that the licensee follows the directions of an authorized user physician.

(2) The actions authorized in paragraph (i)(1) of this section are permitted in spite of more restrictive language in license conditions.

(3) Nothing in this section relieves the licensee from complying with other applicable NRC, FDA, and other Federal or State regulations.

PART 35 - MEDICAL USE OF BYPRODUCT MATERIAL

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

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

For the purposes of sec. 223, 68 Stat. 958, as amended (42 U.S.C. 2273); §§ 35.11, 35.13, 35.20(a) and (b), 35.21(a) and (b), 35.22, 35.23, 35.25,

35.27(a), (c) and (d), 35.31(a), 35.32(a), 35.49, 35.50(a)-(d), 35.51(a)-(c), 35.53(a)-(b), 35.59(a)-(c), (e)(1), (g) and (h), 35.60, 35.61, 35.70(a)-(f), 35.75, 35.80(a)-(e), 35.90, 35.92(a), 35.120, 35.200(b) and (c), 35.204(a) and (b), 35.205, 35.220, 35.300, 35.310(a), 35.315, 35.320, 35.400, 35.404(a), 35.406(a) and (c), 35.410(a), 35.415, 35.420, 35.500, 35.520, 35.605, 35.606, 35.610 (a) and (b), 35.615, 35.620, 35.630(a) and (b), 35.632(a)-(f), 35.634(a)-(e), 35.636(a) and (b), 35.641(a) and (b), 35.643(a) and (b), 35.645(a) and (b), 35.900, 35.910, 35.920, 35.930, 35.932, 35.934, 35.940, 35.941, 35.950, 35.960, 35.961, 35.970, and 35.971 are issued under sec. 161b, 68 Stat. 948, as amended (42 U.S.C. 2201(b)); and §§ 35.14, 35.21(b), 35.22(b), 35.23(b), 35.27(a) and (c), 35.29(b), 35.32(b)-(f), 35.33(a)-(b), 35.36(b), 35.50(e), 35.51(d), 35.53(c), 35.59(d), (e)(2), (g), and (i), 35.70(g), 35.80(f), 35.92(b), 35.204(c), 35.310(b), 35.315(b), 35.404(b), 35.406(b) and (d), 35.410(b), 35.415(b), 35.610(c), 35.615(d)(4), 35.630(c), 35.632(g), 35.634(f), 35.636(c), 35.641(c), 35.643(c), 35.645, and 35.647(c) are issued under sec. 161o, 68 Stat. 950, as amended (42 U.S.C. 2201(o)).

4. In § 35.200, paragraph (c) is revised to read as follows:

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

* * * * *

(c)(1) From August 23, 1990, to August 23, 1993, a licensee may depart from the manufacturer's instructions for eluting generators and preparing reagent kits for which the Food and Drug Administration (FDA) has approved a

"New Drug Application" (NDA), by following the directions of an authorized user physician.

(2) Nothing in this section relieves the licensee from complying with other applicable NRC, FDA, and other Federal or State regulations.

5. In § 35.300, paragraph (b) is revised to read as follows:

§ 35.300 Use of radiopharmaceuticals for therapy.

* * * * *

(b)(1) From August 23, 1990, to August 23, 1993, a licensee may depart from the package insert instructions regarding indications or method of administration for a radiopharmaceutical for which the Food and Drug Administration (FDA) has approved a "New Drug Application" (NDA), provided that the authorized user physician has prepared a written directive as required by § 35.32(a).

(2) Nothing in this section relieves the licensee from complying with other applicable NRC, FDA, and other Federal or State regulations.

Dated at Rockville, Maryland, this _____ day of _____ 1992.

For the Nuclear Regulatory Commission.

_____
James M. Taylor,
Executive Director for Operations.

DOC. FILE NAME: PT35.TMP

LONG DISPLAY: Departures from Mfrs Instructions

CREATED:

AUTHOR: SJones

REVISED:	08/28/92	08/28/92	09/01/92	09/02/92	09/04/92
TYPIST:	C. Jones	CJ	CJ	CJ	CJ
TIME:	3:30 pm	3:25 pm	10:30 am	10:45 am	2:30 pm

EXCERPT:

[7590-01]

NUCLEAR REGULATORY COMMISSION

10 CFR Parts 30 and 35

RIN: 3150 - AE23

Departures From Manufacturer's Instructions;
Elimination of Recordkeeping Requirements

Enclosure 2

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

The Honorable Peter H. Kostmayer, Chairman
Subcommittee on Energy and the Environment
Committee on Interior and Insular Affairs
United States House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

Enclosed for the information of the subcommittee is a copy of a final rule to be published in the Federal Register.

The Nuclear Regulatory Commission (NRC) is amending its regulations to eliminate certain recordkeeping requirements related to the preparation or use of radiopharmaceuticals. These requirements have been in place since August 23, 1990. Specifically, this rule will eliminate recordkeeping requirements related to the justification for and a precise description of the departure, and the number of departures from the Food and Drug Administration (FDA) approved manufacturer's instructions. The FDA staff, also, has no objection to eliminating these recordkeeping requirements. Both the NRC and the FDA staffs agree that the major trends in departures that may be identified by this recordkeeping are already discernible and collecting additional data is unnecessary.

The estimated reduction in annual burden would be approximately 1000 hours for NRC licensees.

Sincerely,

Dennis K. Rathbun, Director
Office of Congressional Affairs

Enclosure:
Federal Register Notice

cc: Representative John J. Rhodes