

UNITED STATES
NUCLEAR REGULATORY COMMISSION
OFFICE OF NUCLEAR MATERIAL SAFETY AND SAFEGUARDS
WASHINGTON, D.C. 20555

September 29, 1994

NRC INFORMATION NOTICE 94-70: ISSUES ASSOCIATED WITH USE OF
STRONTIUM-89 AND OTHER BETA
EMITTING RADIOPHARMACEUTICALS

Addressees

All U.S. Nuclear Regulatory Commission Medical Licensees.

Purpose

The U.S. Nuclear Regulatory Commission is issuing this information notice to alert its licensees of the following:

- A. special considerations for assaying pure beta emitting radiopharmaceuticals;
- B. safety considerations for managing patients who have been treated with therapeutic dosages of beta emitting radiopharmaceuticals; and
- C. physician training and experience requirements for the therapeutic use of radiopharmaceuticals other than I-131 (i.e., strontium-89, rhenium-186, samarium-153).

It is expected that recipients will review this information for applicability to their facilities and consider actions, as appropriate. However, suggestions contained in this information notice do not represent new NRC requirements; therefore, no specific actions or written response is required.

Description of Circumstances

The use of therapeutic quantities of pure beta emitting radioisotopes may pose special technical difficulties. These difficulties include assaying of the radiopharmaceutical dosages and determining the isotope burden of the patient. Furthermore, opening of the body cavity or exposure to body fluids encountered in surgery, autopsy, embalming, or cremation may require special precautions to limit the possible spread of contamination from the radioisotope present in the patient.

Strontium-89 (Sr-89) Metastron has an approved New Drug Application (NDA) from the Food and Drug Administration (FDA) for use in therapeutic amounts to reduce bone pain from metastatic bone lesions. Other beta emitting radionuclides such as rhenium-186 (Re-186) and samarium-153 (Sm-153) are currently under review by the FDA for similar approval. Section 35.300 of

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10 CFR Part 35 authorizes the therapeutic use of Sr-89 Metastron since an NDA has been approved by the FDA.

However, the physician training and experience requirements for the use of Sr-89 or other pure beta emitting radionuclides are not explicitly addressed in 10 CFR Part 35. Therefore, this document explains the training and experience criteria for the therapeutic use of radiopharmaceuticals, other than I-131.

Discussion

Assaying Dosages:

Subpart C of 10 CFR Part 35 does not require the use of a dose calibrator to measure patient dosages of radiopharmaceuticals containing pure beta emitters. However, it is our understanding that the manufacturer of Sr-89 Metastron has participated in intercomparisons with the National Institutes of Standards and Technology (NIST) in the calibration of its beta measurement instruments. Therefore, until appropriate measuring instruments and standards are developed and available, reliance on the manufacturer's stated activity of the unit dosage may be the most accurate means, and an acceptable method, of determining the activity of the patient dosage.

A licensee may use a dose calibrator to accurately measure the patient dosage containing pure beta emitters; however, there are inherent technical difficulties to overcome. These difficulties include, but are not limited to, dependence upon geometry, lack of an industry standard for the materials used in the manufacture of both vials and syringes, and a lack of a suitable Sr-89 calibration standard from NIST. For example, if there is a need to administer an activity different from the unit dosage supplied by the manufacturer, the licensee should perform either a volumetric adjustment based on the manufacturer's stated specific activity, or use the appropriate setting on a dose calibrator specifically designed and calibrated to measure beta activity. If the latter method is used, you should assay patient dosages in the same type of vial and geometry as used to determine the correct dose calibrator settings. The use of different vials or syringes may result in measurement errors due to the variation of bremsstrahlung created by interaction between beta rays and the differing dosage containers. Licensees are reminded that beta emitters should be shielded using a low-atomic-numbered material to minimize the production of bremsstrahlung, followed by a high-atomic-numbered material thick enough to attenuate the bremsstrahlung intensity.

NRC recently became aware of a case where a licensee inadvertently administered a therapeutic dose of Sr-89 to a patient when a diagnostic dose of a different radiopharmaceutical was intended. Licensees may want to develop a method for distinguishing between therapy and diagnostic doses, such as physical separation or using a different colored label.

If the procedures in your Quality Management Program (QMP) state that you will measure radiopharmaceuticals for therapy in a dose calibrator, you should either continue to measure the dosage in the dose calibrator after determining the appropriate dose calibrator setting or modify the QMP to state that you

will rely on the manufacturer's calibration for unit dosages. Licensees are reminded that modifications to the QMP must be furnished to the appropriate NRC Regional Office within 30 days after the modification has been made (§35.32(e)).

In addition, the proposed radiopharmacy rule published in the Federal Register, June 17, 1993, would require medical use licensees to measure dosages of alpha- and beta-emitting radionuclides, except for unit dosages obtained from the manufacturer or commercial nuclear pharmacy. Also, the proposed rule would allow a licensee to use a combination of measurements and calculations to determine the dosage of alpha- or beta-emitting radionuclides. It is anticipated that the final rule, which is scheduled to be approved by the Commission prior to issuance, will be published by early 1995.

Managing Patients:

Due to the long half-life of some alpha- or beta-emitting radionuclides, contamination of hospital or funeral home personnel and facilities, in the event of surgery or death following administration of these radiopharmaceuticals, is possible. Licensees administering radiopharmaceuticals containing Sr-89, or other long lived isotopes, may wish to review NCRP Report No. 37, *Precautions in the Management of Patients Who Have Received Therapeutic Amounts of Radionuclides*, for guidance in managing these patients. Although the report does not specifically address Sr-89, it does provide a guide for persons concerned with care of patients who have received therapeutic dosages of radionuclides. Copies of this publication can be obtained by writing:

National Council on Radiation Protection and Measurements
7910 Woodmont Avenue
Bethesda, MD 20814

or, by phoning the NCRP at (301) 657-2652. Currently, the price is \$20.00 plus \$3.00 postage.

The main source of exposure to workers handling deceased patients who have been administered Sr-89 (half-life of 50.5 days) is contamination from contact with body fluids. Using extremely conservative assumptions, an estimated skin dose to workers handling deceased patients was calculated by NRC staff. The calculations were based on the typical administered dosage of 4.05 mCi (150 MBq). Assuming that all of the activity was in the blood and the patient died immediately, the skin dose to a worker not wearing gloves was estimated to be 447 mrad (4.47×10^{-3} Gy) per hour. Assuming the worker was contaminated with body fluids and worked for 4 hours with the patient, the skin dose would be about 1.8 rad (0.18 Gy). If the worker wears gloves, the skin dose is reduced to 180 mrad (1.8×10^{-3} Gy) per hour, which gives a skin dose of 720 mrad (7.2 Gy) when handling a patient for 4 hours. These skin doses are within regulatory limits; however, all necessary precautions should be taken to minimize the dose as much as possible. In fact, most patients do not die immediately after receiving Sr-89, and the Sr-89 is rapidly taken up in the extracellular fluid and intracellularly, primarily in the skeleton with less than 1 percent of the dosage present in the blood at 140 hours (about 6

days).¹ Therefore, any skin doses to a worker should actually be much lower than the ones estimated previously. Licensees should use typical precautions, e.g. use of gloves and protective clothing, in preventing contamination when using Sr-89 and other beta emitting radioisotopes for therapy. Workers should wash their hands and change into clean gloves and laboratory coats/gowns if the protective clothing becomes contaminated.

The National Radiological Protection Board in the United Kingdom has performed a radiological assessment to estimate the impact of cremating corpses of people who have received treatment with Sr-89.² The calculations were based on an assumption that the entire dose of 4.05 mCi (150 MBq) was present in the ash. The maximum dose to a crematorium worker would be about 0.01 mrem (0.1 μ Sv) (effective) from inhalation of ash, and about 0.02 mrem (0.2 μ Sv) (effective) from ingestion of ash. Again, these estimates were calculated using conservative assumptions. Normal precautions should be taken in handling the ash as with any other cremation. Workers typically wear protective clothing including barrier face masks or respirators when handling ash.

Training and Experience:

If a physician is currently authorized for the therapeutic use of radiopharmaceuticals, (10 CFR 35.300) and requests authorization for therapeutic use of radiopharmaceuticals other than I-131 (i.e., P-32 or Sr-89), no additional authorization by license amendment from NRC is required. If a physician is NOT currently so authorized by NRC, the training and experience requirements described in 35.930 would apply, i.e., board certification by the American Board of Nuclear Medicine or the American Board of Radiology in radiology or therapeutic radiology; or 80 hours didactic training and supervised clinical experience with 3 case studies involving the radiopharmaceutical for which authorization is requested.

¹International Commission on Radiological Protection, No. 20, "Alkaline Earth Metabolism in Adult Man," Table 29, page 205.

²Contract Report for the National Radiological Protection Board, United Kingdom: Cooper, J.R.; Walmsley, A.; and Charles, D.; "Individual and Collective Doses from the Release of ⁸⁹Sr into the Environment Following Medical Administration; Assessment of the Radiological Impact of the Cremation of Corpses Containing ⁸⁹Sr;" reproduced by A. Wright.

This information notice requires no specific action or written response. If you have questions about the information in this notice, please contact the technical contact listed below or the appropriate regional office.

Carl J. Paperiello
Carl J. Paperiello, Director
Division of Industrial and
Medical Nuclear Safety
Office of Nuclear Material Safety
and Safeguards

Technical contact: Torre Taylor, NMSS
(301) 504-1062

Attachments:

1. List of Recently Issued NMSS Information Notices
2. List of Recently Issued NRC Information Notices

Attachments filed in Jacket.

LIST OF RECENTLY ISSUED
NMSS INFORMATION NOTICES

Information Notice No.	Subject	Date of Issuance	Issued to
94-65	Potential Errors in Manual Brachytherapy Dose Calculations Generated Using a Computerized Treatment Planning System	09/12/94	All U.S. Nuclear Regulatory Commission medical licensees.
94-64	Reactivity Insertion Transient and Accident Limits for High Burnup Fuel	08/31/94	All holders of OLs or CPs for nuclear power reactors and all fuel fabrication licensees.
94-47	Accuracy of Information Provided to NRC during the Licensing Process	06/21/94	All U.S. Nuclear Regulatory Commission Material Licensees.
94-39	Identified Problems in Gamma Stereotactic Radiosurgery	05/31/94	All U.S. Nuclear Regulatory Commission Teletherapy Medical Licensees.
94-38	Results of a Special NRC Inspection at Dresden Nuclear Power Station Unit 1 Following a Rupture of Service Water Inside Containment	05/27/94	All holders of OLs or CPs for NPRs and all fuel cycle and materials licensees authorized to possess spent fuel.
94-37	Misadministration Caused by a Bent Interstitial Needle during Brachytherapy Procedure	05/27/94	All U.S. Nuclear Regulatory Commission Medical Licensees authorized to use brachytherapy sources in high-, medium-, and pulsed-dose-rate remote afterloaders.

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Information Notice No.	Subject	Date of Issuance	Issued to
94-69	Potential Inadequacies in the Prediction of Torque Requirements for and Torque Output of Motor-Operated Butterfly Valves	09/28/94	All holders of OLs or CPs for nuclear power reactors.
94-68	Safety-Related Equipment Failures Caused by Faulted Indicating Lamps	09/27/94	All holders of OLs or CPs for nuclear power reactors.
94-67	Problem with Henry Pratt Motor-Operated Butterfly Valves	09/26/94	All holders of OLs or CPs for nuclear power reactors.
94-66	Overspeed of Turbine-Driven Pumps Caused by Governor Valve Stem Binding	09/19/94	All holders of OLs or CPs for nuclear power reactors.
94-65	Potential Errors in Manual Brachytherapy Dose Calculations Generated Using a Computerized Treatment Planning System	09/12/94	All U.S. Nuclear Regulatory Commission medical licensees.
94-64	Reactivity Insertion Transient and Accident Limits for High Burnup Fuel	08/31/94	All holders of OLs or CPs for nuclear power reactors and all fuel fabrication licensees.
94-63	Boric Acid Corrosion of Charging Pump Casing Caused by Cladding Cracks	08/30/94	All holders of OLs or CPs for pressurized water reactors.
94-62	Operational Experience on Steam Generator Tube Leaks and Tube Ruptures	08/30/94	All holders of OLs or CPs for pressurized water reactors.
94-61	Corrosion of William Powell Gate Valve Disc Holders	08/25/94	All holders of OLs or CPs for nuclear power reactors.

OL = Operating License
 CP = Construction Permit

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Closes IMAB-1523 *see attached concurrence

OFC	IMAB		IMAB		IMAB		Tech Ed		IMOB	
NAME	TTaylor*		LWCamper*		JEGlenn*		EKraus*		FCCombs*	
DATE	09/19/94		8/23/94		8/24/94		4/25/94		9/6/94	
OFC	OGC		DD/IMNS		D/IMNS					
NAME	STreby*		WBrach*		CPaperiello*					
DATE	9/14/94		09/19/94		09/19/94					

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OFC	OGC		DD/IMNS	C	D/IMNS	C			
NAME	STreby*		NBrach		Paperiello				
DATE	9/14/94		9/19/94		9/19/94				

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