



UNITED STATES
NUCLEAR REGULATORY COMMISSION
WASHINGTON, D.C. 20555-0001

June 1, 2018

MEMORANDUM TO: James M. Trapp, Director
Division of Nuclear Materials Safety
Region I

John B. Giessner, Director
Division of Nuclear Materials Safety
Region III

Troy W. Pruett, Director
Division of Nuclear Materials Safety
Region IV

FROM: Theresa V. Clark, Acting Director **/RA/**
Division of Materials Safety, Security, State,
and Tribal Programs
Office of Nuclear Material Safety
and Safeguards

SUBJECT: LICENSING OF LUTETIUM-177

On January 26, 2018, the U.S. Food and Drug Administration (FDA) approved a radiopharmaceutical (LUTATHERA®) that uses lutetium-177 (Lu-177) to treat gastroenteropancreatic neuroendocrine tumors (GEP-NETs). Lu-177 has a half-life of 6.7 days and is delivered in a similar manner as other beta-emitting therapy parenteral administrations. Lu-177 has a short penetration radius, which makes it suitable for radioimmunotherapy for smaller tumors like GEP-NETs. Lu-177 has both gamma and beta emissions, allowing for the acquisition of images incidental to the intended therapeutic treatment.

The U.S. Nuclear Regulatory Commission (NRC) staff reviewed the radiation safety and regulatory aspects (e.g., radionuclide and progeny emissions, radiation detection, monitoring and measurements, authorized user training and experience needs, patient administration and release considerations, dose delivery, handling and waste disposal) of the medical use of Lu-177 and has determined that the applicable licensing provisions are in Title 10 of the *Code of Federal Regulations* (10 CFR) Part 35, Subpart E, "Unsealed Byproduct Material – Written Directive Required." The medical use of Lu-177 is similar to other commonly used beta- and photon-emitting therapeutic radiopharmaceuticals.

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The NRC staff concluded that physicians approved for the use of any beta emitter or any photon-emitting radionuclide with a photon energy less than 150 keV under 10 CFR 35.390, "Training for use of unsealed byproduct material for which a written directive is required" may also be authorized for the medical use of Lu-177. Physicians authorized under 10 CFR 35.396, "Training for the parenteral administration of unsealed byproduct material requiring a written directive," may also be authorized for the medical use of Lu-177.

The NRC staff evaluated waste storage issues when handling Lu-177. Lu-177 waste may be decayed in storage under the performance-based rule in 10 CFR 35.92, "Decay-in-storage." Small quantities of metastable Lu-177 (Lu-177m), with a half-life of 161 days, may be present as a contaminant generated from the production of Lu-177. If present, Lu-177m may contribute approximately 0.02 percent of the total amount of Lu-177. Lu-177m emits low-energy photons and beta emissions that, even in low quantities, are detectable using standard scintillator detectors and Geiger counters. If Lu-177m is detected by appropriate survey methods, then licensees must dispose of the waste material as low-level radioactive waste in accordance with the requirements in 10 CFR Part 20 Subpart K, "Waste Disposal." Further, the licensee would need to develop safe handling and disposal procedures for detectable quantities of Lu-177m.

If the NRC becomes aware of future developments related to the production, distribution, or medical use of Lu-177 that may negatively impact radiation safety, the NRC staff will consider revisiting this licensing approach for any additional actions.

Enclosure:
Radiation Safety Considerations for
Lutetium-177 (Lu-177)

SUBJECT: MEMO TO THE REGIONS RE: LICENSING FOR LUTETIUM-177
DATED: JUNE 1, 2018.

ML18136A824

OFC	MSST/MSEB	MSST/MSEB	MSST/MSEB	OGC	MSST
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DATE	5/17/18	5/17/18	5/17/18	5/24/18	6/01/18

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Radiation Safety Considerations for Lutetium-177 (Lu-177)

Lu-177 is made either by direct neutron irradiation of Lu-176 targets (Lu-176 (n, γ) reaction) or indirectly as a decay product of the neutron irradiation of ytterbium-176 (Yb-176) (Yb-176(n, γ) reaction), which produces Yb-177 that decays to Lu-177. In the indirect reaction, no long-lived contaminants are created; however, in the direct reaction, small quantities of metastable Lu-177 (Lu-177m) with a half-life of 161 days may be present. If present, Lu-177m may contribute approximately 0.02 percent of the total amount of Lu-177, which equates to approximately 160 μ Ci in a typical patient dosage of 800 mCi (200 mCi per four doses) in a complete LUTATHERA[®] treatment cycle.

Under normal circumstances, minimal Lu-177m waste will be generated since the majority of the dose is injected into the patient. However, any non-administered Lu-177 could result in a buildup of Lu-177m waste. Lu-177m cannot be decayed in storage under the performance-based rule in 10 CFR 35.92, "Decay-in-storage," because its half-life is greater than 120 days. Therefore, licensees must dispose of detectable Lu-177m waste as low-level radioactive waste in accordance with 10 CFR Part 20 Subpart K, "Waste Disposal."

Licensees should establish precautions for managing patients that are hospitalized and should provide patient instructions for those that are released. These provisions are important given potential Lu-177 contamination from the typical excretion of 60 to 80 percent of the administered dose in a few hours after radiopharmaceutical administration.

The information contained in this memorandum is applicable to Lu-177 labelled products other than Lu-177 dotatate (primarily, LUTATHERA[®]).



UNITED STATES
NUCLEAR REGULATORY COMMISSION
WASHINGTON, D.C. 20555-0001

June 21, 2018

ALL AGREEMENT STATES, VERMONT, WYOMING

LICENSING OF LUTETIUM-177 (STC-18-042)

Purpose: To inform Agreement States of the U.S. Nuclear Regulatory Commission (NRC) Lutetium-177 (Lu-177) licensing decision.

Background: On January 26, 2018, the U.S. Food and Drug Administration (FDA) approved a radiopharmaceutical (LUTATHERA[®]) that uses lutetium-177 (Lu-177) to treat gastroenteropancreatic neuroendocrine tumors (GEP-NETs). Lu-177 has a half-life of 6.7 days and is delivered in a similar manner as other beta-emitting therapy parenteral administrations. Lu-177 has a short penetration radius, which makes it suitable for radioimmunotherapy for smaller tumors like GEP-NETs. Lu-177 has both gamma and beta emissions, allowing for the acquisition of images incidental to the intended therapeutic treatment.

Discussion: The NRC staff reviewed the radiation safety and regulatory aspects (e.g., radionuclide and progeny emissions, radiation detection, monitoring and measurements, authorized user training and experience needs, patient administration and release considerations, dose delivery, and handling and waste disposal) of the medical use of Lu-177 and has determined that the applicable licensing provisions are in Title 10 of the *Code of Federal Regulations* (10 CFR) Part 35, Subpart E, "Unsealed Byproduct Material – Written Directive Required." The medical use of Lu-177 is similar to other commonly used beta- and photon-emitting therapeutic radiopharmaceuticals.

The NRC staff concluded that physicians approved for the use of any beta emitter or any photon-emitting radionuclide with a photon energy less than 150 keV under 10 CFR 35.390, "Training for use of unsealed byproduct material for which a written directive is required" may also be authorized for the medical use of Lu-177. Physicians authorized under 10 CFR 35.396, "Training for the parenteral administration of unsealed byproduct material requiring a written directive," may also be authorized for the medical use of Lu-177.

The NRC staff evaluated waste storage issues when handling Lu-177. Lu-177 waste may be decayed in storage under the performance-based rule in 10 CFR 35.92, "Decay-in-storage." Small quantities of metastable Lu-177 (Lu-177m), with a half-life of 161 days, may be present as a contaminant generated from the production of Lu-177. If present, Lu-177m may contribute approximately 0.02 percent of the total amount of Lu-177. Lu-177m emits low-energy photons and beta emissions that, even in low quantities, are detectable using standard scintillator detectors and Geiger counters. If Lu-177m is detected by appropriate survey methods, then licensees must dispose of the waste material as low-level radioactive waste in accordance with the requirements in 10 CFR Part 20 Subpart K, "Waste Disposal." Further, the licensee would need to develop safe handling and disposal procedures for detectable quantities of Lu-177m.

Additional radiation safety considerations for Lu-177 can be found using NRC's Agencywide Documents Access and Management System Accession No. ML18136A824. If the NRC becomes aware of future developments related to the production, distribution, or medical use of Lu-177 that may negatively impact radiation safety, the NRC staff will consider revisiting this licensing decision for any additional actions.

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SUBJECT: LICENSING OF LUTETIUM-177

ML18156A589

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