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

December 8, 2022

MEMORANDUM TO: Anne DeFrancisco, Chief
Medical & Licensing Assistance Branch
Division of Radiological Safety and Security
Region I

Joseph Nick, Acting Chief
Materials Licensing Branch
Division
of Radiological Safety and Security
Region III

Neil O'Keefe
Materials Licensing Branch
Division of Radiological Safety and Security
Region IV

FROM: Christian Einberg, Chief
Medical Safety and Events Assessment Branch
Division of Materials Safety, Security, State,
and Tribal Programs
Office of Nuclear Material Safety
and Safeguards

Signed by Einberg, Christian
on 12/08/22

SUBJECT: REVISION OF 2018 MEMORANDUM TO THE REGIONS, "LICENSING OF LUTETIUM-177"

On June 1, 2018, the U.S. Nuclear Regulatory Commission (NRC) issued a memorandum to the Regions (Agencywide Documents Access and Management System Accession No. ML18136A824) regarding the medical use of lutetium-177 (Lu-177) following an approval by the U.S. Food and Drug Administration (FDA) of LUTATHERA® (Lutetium-177 dotatate), a radiopharmaceutical that uses Lu-177 to treat gastroenteropancreatic neuroendocrine tumors (GEP-NETs). On March 23, 2022, the FDA approved another Lu-177 radiopharmaceutical, PLUVICTO™ (Lutetium-177 vipivotide tetraxetan) for the treatment of prostate-specific membrane antigen positive metastatic castration-resistant prostate cancer. The NRC staff reviewed the use of PLUVICTO™ and found that all radiation safety considerations within the 2018 memorandum apply to PLUVICTO™. This 2022 memorandum supersedes the 2018 memorandum.

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Lu-177 has a half-life of 6.7 days. Lu-177 beta emissions have a short penetration radius, which makes it suitable for radioimmunotherapy. Lu-177 has both gamma and beta emissions, allowing for the acquisition of images incidental to the intended therapeutic treatment. LUTATHERA® and PLUVICTO™, both Lu-177 radioimmunotherapy radiopharmaceuticals are delivered similarly to other approved beta-emitting therapy parenteral administrations.

The NRC staff reviewed 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 medical uses of Lu-177 radioimmunotherapy radiopharmaceuticals (i.e., LUTATHERA® and PLUVICTO™) and determined that applicable licensing provisions are within Title 10 of the *Code of Federal Regulations* (10 CFR) Part 35, Subpart E, “Unsealed Byproduct Material – Written Directive Required.”

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. Additionally, 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 and storage issues when handling Lu-177, LUTATHERA® and PLUVICTO™. 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 survey methods, then it must be disposed as low-level radioactive waste in accordance with the requirements in 10 CFR Part 20 Subpart K, “Waste Disposal.” Furthermore, 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 uses of Lu-177 radiopharmaceuticals that may negatively impact radiation safety, the NRC staff will consider revisiting this licensing decision.

Memo to Regions, REVISION OF 2018 MEMORANDUM TO THE REGIONS, "LICENSING OF LUTETIUM-17" DATE December 8, 2022

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