



HEALTH PHYSICS SOCIETY

Specialists in Radiation Safety

October 14, 2020

Secretary
U.S. Nuclear Regulatory Commission
Washington, DC 20555-0001
ATTN: Rulemakings and Adjudications Staff
Email to: Rulemaking.Comments@nrc.gov

Eric Goldin, Ph.D., CHP
President

Subject: Docket ID [NRC-2020-0141](#) - Reporting Nuclear Medicine Injection Extravasations as Medical Events

The Health Physics Society¹ (HPS) is a professional organization whose mission is to promote excellence in the science and practice of radiation safety. The HPS appreciates the opportunity to provide comments, in the attached document, as a response to the September 15, 2020 request.

If you have any questions regarding these comments, please contact the HPS Agency Liaison, Craig Little, at 970-260-2810 or by email to agencyliaison@hps.org.

Sincerely,

Eric Goldin, PhD, CHP
President

cc: Craig Little, PhD, HPS Agency Liaison
Brett Burk, HPS Executive Director

¹ The Health Physics Society is a non-profit scientific professional organization whose mission is to promote the practice of radiation safety. Since its formation in 1956, the Society has grown to include over 4,000 scientists, physicians, engineers, lawyers, and other professionals representing academia, industry, government, national laboratories, the Department of Defense, and other organizations. Society activities include encouraging research in radiation science, developing standards, and disseminating radiation safety information. Society members are involved in understanding, evaluating, and controlling the potential risks from radiation relative to the benefits. Official position statements are prepared and adopted in accordance with standard policies and procedures of the Society.

Health Physics Society Comments on Reporting Nuclear Medicine Injection Extravasations as Medical Events

Position Details

As a scientific organization of professionals who specialize in radiation safety, the HPS does not believe the infiltration/extravasation of radiopharmaceuticals should be classified as a Medical Event. Infiltration of a portion of the radiopharmaceutical is often unavoidable, and in the case of sentinel node imaging, is even intentional. Labeling an infiltration as a Medical Event carries a fairly serious stigma, and yet there is no evidence that infiltration of radiopharmaceuticals carries any health consequences for the patient or the general public.

As detailed in the NRC's Advisory Committee on Medical Use of Isotopes (ACMUI)², the purpose of reporting Medical Events was for the NRC to evaluate if there is a breakdown in the licensee's program for ensuring that byproduct material or radiation from byproduct material was administered as directed by the Authorized User (AU), or if there was a generic issue that should be reported to other licensees, that could lead to reduced likelihood of other medical events and enhanced radiological safety. The report acknowledges that extravasation frequently occur in normal intravenous procedures and are almost impossible to prevent. Such events are inconsistent with the stated purpose of a Medical Event.

If NRC considers extravasation a Medical Event, such a classification could force the estimation of the localized dose. Accurate measurement may require serial CT imaging of the site, which may result in additional patient dose simply for the purpose of complying with a regulation. This additional imaging would add substantially to the costs of doing any procedure, including facility, technologist, and physician time. Additional documentation of the survey and measurement of infiltration would need to be included in the medical record, adding further to additional burden and raising the issue of needlessly alarming patients.

We note that the skin has a relatively low stochastic radiation risk, with a weighting factor of only 0.01 in the ICRP 103 methodology. It is our opinion that attributable stochastic risk from an infiltration is relatively unimportant in the context of the patient's radiation exposure from other diagnostic or therapeutic exposures. The focus for intervention and patient safety should be on the potential tissue reaction aspects of these incidents. In this context, more appropriate triggers for whether a Medical Event occurred than the use of the 0.5 Sv (50 rem) Medical Event limit should apply. For example, transient erythema from fluoroscopic x-rays is thought to have a relative threshold of 2 Gy (200 rad), with higher dose leading to increased injury. The Conference of Radiation Control Program Directors (CRCPD) recommends guidance for managing fluoroscopy skin doses in [PART F MEDICAL DIAGNOSTIC AND INTERVENTIONAL X-RAY AND IMAGING SYSTEMS](#). The suggested state regulations use the guidance of the American

² Nuclear Regulatory Commission (NRC) Advisory Committee on the Medical Use of Isotopes (ACMUI) Subcommittee on Extravasation, Final Report. April 6, 2020.

College of Radiology Technical Standard on managing radiation exposure in fluoroscopic procedures³. This technical standard recommends monitoring for and medically managing possible radiation effects when the dose reaches 5 Gy at the interventional reference point, a value approximating a 2 Gy skin dose

Patients routinely undergo procedures that entail potentially much higher than 0.5 Sv (50 rem) doses to skin in fluoroscopy procedures, which may or may not be optimized or tracked, and for which the consensus is that the dose to this tissue is not risk significant with respect to stochastic effects when considered in the context that includes the patient's dose from the rest of their care. When skin effects are seen (> 2 Gy) with escalating potential injury at higher doses), they are medically managed. This practice is consistent with the ICRP principles of justification and optimization.

We believe that continued close attention should be paid to avoid infiltration of ALL parenterally administered radiopharmaceuticals. We also acknowledge the specific concerns associated with the infusion of therapeutic agents and that extravasation of a therapeutic dosage of a radiopharmaceutical can result in potentially injurious radiation exposure to localized tissue. Oversight of therapy effects should also be considered in the context of the patient's care and may be more appropriately managed skin effects are in complex fluoroscopy cases⁴. Where feasible the dose should be estimated, but it should be recognized that there may be substantial barriers to doing so and that a specific dose determination may not have a significant impact on clinical management. In any case, appropriate medical intervention should be undertaken and that such incidents should be reported to the Radiation Safety Officer, Radiation Safety Committee and to the appropriate patient safety organization. It is unclear whether classifying infiltrations / extravasations, incidents which may be unavoidable, as a Medical Event best serves the interest of health and safety.

Response to specific questions:

NRC question: *How frequently does radiopharmaceutical extravasation occur?*

Extravasation is estimated to occur in 0.6% to 6% of radiopharmaceutical administrations^{5,6}. In nuclear medicine however, there appear to be relatively few reports of side effects from extravasation of radiotherapeutic agents, and no reports of side effects related to extravasation of diagnostic agents (with regard to localized radiation dose)⁷.

³ American College of Radiology. ACR-AAPM [Technical Standard](#) for Management of the Use of Radiation in Fluoroscopic Procedures.

⁴ The Joint Commission. Sentinel Event Alert 47: Radiation risks of diagnostic imaging and fluoroscopy. August 24, 2011. Revised February 2019.

⁵ van der Pol J, Vöö S, Bucerius J, Mottaghy, F. Consequences of radiopharmaceutical extravasation and therapeutic interventions: a systematic review. *Eur J Nucl Med Mol Imaging* (2017) 44:1234–1243.

⁶ Jordan K, Grothe W, Schmoll HJ. Extravasation of chemotherapeutic agents: prevention and therapy. *Dtsch Med Wochenschr.* 2005;130:33–37.

⁷ Rhymer S, Parker JA, and Matthew R. Palmer M. Detection of 90Y Extravasation by Bremsstrahlung

NRC question: *For medical use licensees, does your facility currently monitor for radiopharmaceutical extravasation? If so, why and how do you monitor? If not, why not?*

Nuclear medicine clinics currently monitor for radiopharmaceutical extravasation. To reduce the risk of extravasation many clinics administer radiopharmaceuticals through an IV-catheter that has been test flushed to ensure patency while visually inspecting if swelling occurs and asking the patient if they experience discomfort during injection⁸. However, even with such precautions an extravasation may not be identified until the patient is imaged⁹.

NRC question: *Do you expect that monitoring for extravasation and reviewing the results would improve radiopharmaceutical administration techniques at medical use licensee facilities? If so, how? If not, why not?*

The techniques identified above reduce the number of extravasations during administration and existing reporting to the hospital quality assurance programs already provide oversight of the number of extravasations. Extravasations in nuclear medicine administrations are low in comparison to chemotherapy administrations, where the extravasation rate may be as high as 35 to 50%¹⁰.

As stated by NRC's Advisory Committee on the Medical Use of Isotopes (ACMUI), "The prevention of extravasation is a medical training issue for the authorized user (AU) physician and the technologist under the supervision of the AU, which is considered medical practice and not something that needs NRC regulation."¹¹

Adding NRC oversight of extravasations will increase the regulatory burden without a radiological or patient safety benefit.

NRC question: *Do you believe an NRC regulatory action requiring monitoring and review of extravasation would improve patient radiological health and safety? If so, how? If not, why not?*

Imaging for Patients Undergoing ⁹⁰Y-Ibritumomab Tiuxetan Therapy. J Nucl Med Technol 2010; 38:195–198.

⁸ van der Pol J, Vöö S, Bucerius J, Mottaghy, F. Consequences of radiopharmaceutical extravasation and therapeutic interventions: a systematic review. Eur J Nucl Med Mol Imaging (2017) 44:1234–1243.

⁹ Qutbi M. Masking Effect of Radiopharmaceutical Dose Extravasation During Injection on Myocardial Perfusion Defects During SPECT Myocardial Perfusion Imaging: A Potential Source of False Negative Result. Mol Imaging Radionucl Ther 2018;27:141-143.

¹⁰ Nickel B. Peripheral Intravenous Access: Applying Infusion Therapy Standards of Practice to Improve Patient Safety. Crit Care Nurse 2019 Feb;39(1):61-71.

¹¹ Nuclear Regulatory Commission (NRC) Advisory Committee on the Medical Use of Isotopes (ACMUI) Subcommittee on Extravasation, Final Report. October 23, 2019.

Regulatory action requiring monitoring and review of extravasations is fundamentally different from the majority of NRC specified medical events that can be attributed to failures to properly identify the patient, to execute the treatment plan, or failure to implant sources in the correct location – all of which are readily preventable.

Monitoring the rate of extravasations is a medical issue that is overseen by the institution's quality management program. Additional regulatory action would only add regulatory burden without an improvement for patient radiological health and safety.

Designating extravasations as a Medical Event would call for a dose estimation, which is far from a trivial process. Use of simplified techniques^{12,13} do not effectively account for removal of the pharmaceutical from the injection site and the time varying geometry of the source, though they can be modified to do so with additional data collection. Simplified techniques can lead to large over-estimates of dose and potentially the number of Medical Events. More accurate evaluations require specific imaging of the patient, including the possible use of SPECT/CT (wherein the CT will contribute additional exposure with arguably minimal to no benefit), or Planar imaging to assess basic clearance from the infiltration site. These assessments require multiple time points, use staff and camera time, and inconvenience the patient who may be unwilling to comply with the additional time commitments and imaging. In hospitalized patients, the additional transportation of patients to and from the imaging suite will require additional hospital resources and may include additional medical risk. In addition, planar imaging alone is not likely to provide useful information regarding the volume of the infiltrate – which itself is time varying as the pharmaceutical is absorbed and translocates. If the licensee is held to a traditional 0.5 Sv trigger for medical events, the choice will be between investing the resources to show that infiltration is below this level, or relying on simplified techniques that will likely lead to an inflated count of medical events.

NRC question: *Are there any benefits, not related to medical techniques, to monitoring and reporting certain extravasations as medical events? What would be the burden associated with monitoring for and reporting certain extravasations as medical events?*

While we do not believe it is appropriate to classify extravasations as medical events, some oversight and trending is appropriate to ensure patient safety. For an extravasated radiopharmaceutical, the Authorized User should promptly take the appropriate medical

¹² Shapiro B. Dosimetric consequences of interstitial extravasation following IV administration of a Radiopharmaceutical. Eur J Nucl Med (1987) 12:522-523.

¹³ Castronovo FP, McKusick KA, and Strauss HW. The infiltrated radiopharmaceutical injection: Dosimetric considerations. Eur J Nucl Med (1988) 14:93-97.

intervention and report the incident to the Radiation Safety Officer and, where applicable the Radiation Safety Committee, as well as to the appropriate patient safety organization.

NRC question: *If the NRC were to require that licensees report certain extravasations as medical events (recorded in NMED), what reporting criteria should be used to provide the NRC data that can be used to identify problems, monitor trends, and ensure that the licensee takes corrective action(s)?*

The focus for intervention and patient safety should be on the potential tissue reaction aspects of these incidents. In this context, more appropriate triggers for whether a medical event has occurred than the use of the 0.5 Sv limit should apply. For example, transient erythema from fluoroscopic x-rays is thought to have a relative threshold of 2 Gy (200 rad), with higher dose leading to increased injury. Perhaps NRC should consider how the Medical Community handles fluoroscopic skin injury¹⁴ if reassessing reporting of extravasations.

NRC question: *If the NRC requires reporting of extravasations that meet medical event reporting criteria, should a distinction be made between reporting extravasations of diagnostic and therapeutic radiopharmaceuticals? If so, why? If not, why not?*

In reviewing how to approach radiopharmaceutical extravasations, the NRC should consider how medicine monitors extravasations of chemotherapy agents. The response to these events focuses on identification and mitigation of physical injury through a variety of methods.

The NRC should consider the recommendations of ACMUI and not include diagnostic radiopharmaceuticals in any Medical Event program¹⁵. In its 2020 Report, ACMUI wrote that diagnostic administrations should not be considered Medical Events as “None of the total doses in these extravasations meet the NRC’s medical event criteria of a discrepancy of a total dosage of $\pm 20\%$ delivered dose criteria.”¹⁶

Should NRC decide to classify extravasation as a Medical Event, we urge the NRC to focus on therapy administrations where there is a potential for patient harm in the form of tissue reactions. The NRC should consider in its analysis whether dose reconstruction adds value to the medical management of the injury. In its assessment, NRC should also consider that

¹⁴ The Joint Commission. Sentinel Event Alert 47: Radiation risks of diagnostic imaging and fluoroscopy. August 24, 2011. Revised February 2019.

¹⁵ Nuclear Regulatory Commission (NRC) Advisory Committee on the Medical Use of Isotopes (ACMUI) Subcommittee on Extravasation, Final Report. April 6, 2020.

¹⁶ Nuclear Regulatory Commission (NRC) Advisory Committee on the Medical Use of Isotopes (ACMUI) Subcommittee on Extravasation, Final Report. October 23, 2019.

infiltration and extravasation are events that are expected to occur at some frequency in medical practice regardless of interventions and quality initiatives.