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Kevin Williams
Director, Division of Materials Safety, Security, State, and Tribal Programs
U.S. Nuclear Regulatory Commission
Washington, DC 20555-0001

Delivered via email

Dear Kevin:

Additional, unconflicted clinical evidence has become available that is extremely pertinent to rulemaking and the extravasation topic.

Pharmacology Research & Perspectives published a short report, "Treatment of [99mTc]Tc-hydroxy-diphosphonate ([99mTc]Tc-HDP) extravasation using hyaluronidase" on July 25, 2024. This important case illustrates that a large diagnostic radiopharmaceutical extravasation can result in a high absorbed dose to skin and underlying tissue. This extravasation and others like it warrant reporting to the patient and regulatory bodies.

The case report provides other important information pertinent to the ongoing discussion around extravasation reporting and the proposed rule.

1. The radioisotope 99mTc is the most commonly used radioisotope. Since many cardiovascular nuclear medicine procedures require two administrations, technologists likely perform over 20,000,000 administrations of 99mTc in the US every year.
2. The delivered (and extravasated) amount of radioactivity in the case report is similar to or less than the amount of 99mTc used during procedures in the United States.
3. The nuclear medicine center from the case report, like many nuclear medicine centers in the United States, used a butterfly syringe to administer a radiopharmaceutical. This is not the best practice for vascular access.
4. This nuclear medicine center implemented mitigation steps as soon as they were aware they had extravasated the patient. They believed these mitigation steps lowered the dose the patient would have received, had no steps been taken, from 13 Gy to 2-3 Gy.
5. This nuclear medicine center performed dosimetry using a readily available published method. Their findings were consistent with doses found in studies using Monte Carlo simulations. Dosimetry can be done. It is not overly complicated, time consuming or beyond the capability of clinicians.
6. The extravasated administration caused the nuclear medicine procedure to be suboptimal for diagnostic purposes and therefore the procedure needed to be repeated at a later time.
7. The patient's skin and underlying tissue was harmed by this extravasation.

From the information noted above and from discussions with unconflicted experts, we can draw the following conclusions and make several observations.

1. 99mTc is not a harmless isotope. Statements opposed to the reporting of large extravasations from the medical societies and their members (including your ACMUI members) are simply not supported by science. Nuclear medicine professionals need to monitor administrations for extravasations whether they are diagnostic or therapeutic radiopharmaceuticals, assess them when they happen, mitigate them to reduce absorbed

dose, and report large extravasations to patients and appropriate regulatory bodies. Public comments to the NRC and members of Congress made by professional organizations that suggest patients "need not be concerned" with diagnostic radiopharmaceutical extravasations are unethical, incorrect, and seem designed to protect the status quo for clinicians (and their pocketbooks)—not to protect patients.

2. The most consistent way to evaluate extravasations for their severity requires performing dosimetry. Dosimetry can be performed using simple, readily available, and free methods.
3. The most consistent way to evaluate extravasations for potential regulatory reporting would be a comparison of the dosimetry results to an objective, dose-based criterion. Such a simple, clear, unambiguous approach could use the same dose-based threshold that is used for all other medical event reporting.
4. Absent a clear, unambiguous reporting requirement, nuclear medicine professionals will not change their behaviors. Centers that are not handling radioisotopes properly will continue to do so. Patients who are unnecessarily exposed to very high absorbed doses will continue to be exposed. The leadership of the Society of Nuclear Medicine and Molecular Imaging and the Health Physics Society and other societies have been aware of the extravasation issue since these organizations formed. They have been regularly reminded of the topic since 2016, yet we are unaware of even one licensee that has a written mitigation protocol in place for a radiopharmaceutical extravasation. Few centers use best practice vascular access protocols, even though clear clinical evidence shows how best practices can nearly eliminate extravasations.

Professional societies are not alone in providing misinformation about the extravasation topic. Despite repeated attempts by ourselves, patients, and unconflicted experts to encourage the medical staff to think critically about the topic, the proposed rule continues to espouse nonsensical statements that cannot be defended with scientific evidence. Like SECY-22-0043, the proposed rule used incorrect information that does not meet NRC information quality guidelines.

As it relates to an extravasation, medical event reporting exists to identify those events in which human error, lack of training, or lack of quality procedures result in the delivery of a radioactive drug or radionuclide through the wrong route of administration (into healthy tissue versus intravenous) that causes an absorbed dose greater than 50 rem to tissue or 50 rem shallow dose equivalent to skin. The ultimate purpose of medical event reporting is to protect patients by understanding what leads to a mishandling of a medical isotopes and to then sharing that information with other licensees to minimize the chance of that mishandling occurring again. From NRC published information, the following six principles apply to medical event reporting:

- patient harm is not necessary to trigger a medical event report.
- radiation-safety-significance is not a consideration on whether to file a medical event report.
- frequency of occurrence of an issue does not determine medical event reporting.
- medical event reporting uses a risk-informed, objective, dose-based threshold.
- medical event reporting does not depend on other factors beyond patient intervention that are outside the licensees' control.
- NRC does not support using subjective criteria to determine whether to file a medical event report.

In the proposed rule supporting documentation, the medical staff contradicts all six of those well-established NRC principles. The following sentence is a case in point:

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> *"Because available information suggests that extravasations that result in patient harm or otherwise compromise patient care are rare, the NRC does not see a need for a dose-based criterion at this time."*

In addition to violating several NRC principles in one sentence, that statement is bewildering because the NRC staff has seen a list of over 100 peer-reviewed documents that show how extravasations harm patients. They have seen evidence that extravasations do exist and can readily be identified at the time of administration. Based on the number of administrations of radiopharmaceuticals every year in the US, even if just 1% of all administrations result in a large extravasation, over 300,000 patients are being affected. If centers are required to address this issue, there is no reason to believe that they will not improve to the same low extravasation rate found in contrast CT injections (which are performed by nuclear medicine's "sister" department, radiology). The causes of extravasation are well known and well documented outside of nuclear medicine. Furthermore, it is well established that extravasations are almost entirely preventable when training and the latest tools are provided to clinicians. If nuclear medicine is forced to report large extravasations, they should quickly reduce the extravasation rate to 1 in 1000 administrations, and of those, perhaps only 1 in 10 would be large enough to report as medical events. That would reduce the number of large extravasations in the US to 3,000 year.

Here is another example of a NRC-principle violating statement from the proposed rule supporting documentation:

> *"Monitoring millions of administrations per year, which would result in significant regulatory burden for medical licensees for only a marginal increase in radiation safety."*

Monitoring the quality of a medical procedure is not a regulatory burden. Providers spend millions every year to provide high quality care. They just simply don't do it for the administration of radioactive drugs in patients. But if they are required to report large extravasations that exceed existing medical event reporting criteria, they will quickly adopt the solutions other departments in the hospital have used to reduce their extravasation rate. They will drive that rate as close to zero as possible. Furthermore, to the hundreds of thousands of patients who are being adversely affected by nuclear medicine extravasations, the NRC position is offensive. Reducing large extravasations for over 300,000 patients is not a marginal increase in radiation safety—it is the duty of the NRC.

While the supporting information for the proposed rule has many more factual errors, I will address those at a later date. In the meantime, I encourage the staff to read the case report with a critical mind and see how this report affects all that you have heard about this topic.

Sincerely,

Ronald K. Lattanze

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Ronald K. Lattanze

Cc: Christopher Hanson, Chairman
David Wright, Commissioner
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Robert Feitel, Inspector General