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Reporting Nuclear Medicine Injection Extravasations as Medical Events

Comment On: NRC-2020-0141-0004
Reporting Nuclear Medicine Injection Extravasations as Medical Events; Notification of Docketing and Request for Comment

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General Comment

See attached file(s)

Attachments

NRC PRM-35-22 Extravasation Petition Comments-RPLieto

November 30, 2020

Submitted via online

Attn: Pamela Noto
Office of Nuclear Material Safety and Safeguards
U.S. Nuclear Regulatory Commission
Washington, DC 20555-0001

Re: (Docket ID NRC-2020-0141; PRM-35-22) Petition for rulemaking; notification of docketing and request for comment; *Reporting Nuclear Medicine Injection Extravasations as Medical Events*.

I appreciate the opportunity to provide comments to the Nuclear Regulatory Commission (NRC) petition attempting to establish nuclear medicine injections as medical events. I am requesting that the NRC deny this petition because it is intended to benefit the financial interests of the petitioner, misrepresents many of the citations supporting the petition, requires resources not available and impractical to implement in order to obtain the expected quantitative results needed to estimate the petition's absorbed dose limit, and would definitely have a negative impact on the quality and availability of diagnostic nuclear medicine studies.

The following comments and responses to NRC questions are based on my observations as a clinical medical physicist in nuclear medicine and Radiation Safety Officer with almost 40 years of experience with NRC licensees employing multi-modality programs.

The petitioner fails to make an important distinction in the terminology where "extravasation" is inappropriately considered synonymous with "infiltration". Extravasation is that uncommon occurrence where an infiltration causes tissue damage or other injury such as is associated with accidental infiltration of a vesicant or chemotherapeutic drug. Unfortunately, both terms are used interchangeably in this petition. For diagnostic radiopharmaceuticals the absorbed dose from leakage does not meet the threshold for a deterministic effect. Unless the drug itself is a vesicant, it seems that the event should be considered an infiltration and not an extravasation. An infiltration should not require an absorbed dose estimation.

Infiltrations/extravasations, as the NRC's own Advisory Committee on the Medical Use of Isotopes (ACMUI) has repeatedly stated, occur throughout all the fields of medicine where nonradioactive intravenous (IV) administrations are performed. The medical, and especially nursing, literature have documented for decades occurrences and care for these events. In fact, the nursing societies have developed national guidance documents for the management of extravasations [Hadaway L. Infiltration and extravasation: preventing a complication of IV catheterization. Am J Nurs. 2007;107(8):64-72.]. These documents indicate a number of patient conditions that contribute to patient extravasations resulting in leakage into surrounding tissue and are not the result of a "bad stick" needing regulatory control. Such patient conditions are unpreventable and uncontrollable. These causes of such patient conditions, which could be considered "passive patient intervention", include:

- Small vein size
- Poor vein condition including vein porosity or vein fragility
- Venous spasm due to temperature or blood pressure changes
- Clot restricting normal venous blood flow
- Multiple venipuncture sites
- Patient hydration
- Patient movement causing needle to accidently exit the vein by either backing out from the point of insertion or puncturing the other side of the vein.

Patients most prone to extravasations from these causes are those most likely in need of nuclear medicine imaging and treatment administrations – elderly and cancer patients. Importantly, an infiltrated injection can and often times does still result in interpretable diagnostic images. Extravasations cannot be prevented. Even Lucerno's own multicenter study [*Wong et.al., J Nucl Med Technol 2019; 47:326–331*] showed that its device only reduced percent infiltration by 6-7%.

The methodology to assess absorbed dose from the output of the Lucerno Lara device is poorly described and impractical to implement in routine nuclear medicine because it is a lengthy process to accomplish, beyond the capability of nuclear medicine technologists, requires software not used in clinical nuclear medicine departments, and requires input from a very expensive monitor provided by the petitioner. The petitioner has taken essentially the output from a small area scintillation survey meter (counts per second) and converted it to tissue absorbed dose (gray) but provides no description on the methodology in order that it can be independently verified. Critical factors such as volume of the infiltrate and amount of activity in the infiltrate are assumed values, not measured, to provide high absorbed dose estimates which will assure over-reporting of tissue doses. The specific method by which "percent extravasated" is calculated is not described in the petition or its references. The tissue dosimetry provided in the Appendix of the petition is suspect because input factors such as volume of tissue varies by a factor of 20, extravasated activity is estimated up to 100%, and the residence times for the same radiopharmaceutical in the same tissue, which should have small variance, varies by up to a factor of 9. These provide dose estimates that are intended and do provide sensational and excessive tissue doses that far exceed deterministic threshold for skin effects. Notably, none of the subjects exceeding skin effect thresholds are cited as having found any harmful physical effects.

This petition would require that ***every*** IV administration would have an assessment to quantitate size of an infiltration and dose estimate to determine if an arbitrary threshold had been exceeded. This petition fails to recognize the time and resources needed to perform such assessments. This is beyond the scope for technologists, and the software and medical physics resources needed are not available for most nuclear medicine facilities. These assessments can take several hours to days to complete depending on available resources and experience in performing the quantitative dose estimates. Such a mandate as requested in the petition would significantly increase patient study time, adversely affect the availability of imaging equipment, require significant financial resources (software and human), and negatively impact the practice of nuclear medicine.

The petition is asking the NRC to establish a new definition of medical event in order for extravasations to be made reportable and for a purpose for which it was not intended. A medical event is intended to capture those administrations that deviate from the written directive or protocol approved by the Authorized User AND exceeds a dose threshold based on a relevant

dose limit. Nothing in the petition indicates that a deviation from the AU's intention has occurred. In effect, the petitioner is requesting that a tissue dose of an injection site receiving 50 rem be established as medical event even though no deviation from intent has occurred. This is totally unjustifiable. If NRC intends to proceed with such a reckless move, the dose MUST be based on a threshold for possible deterministic effects in skin. However, this may have adverse repercussions because one can make a similar argument for the skin erythema that occurs in teletherapy when the intended dose is properly delivered to an internal tissue/organ.

Responses to NRC Questions

1. How frequently does radiopharmaceutical extravasation occur?

Very rare. If this was frequently occurring as the petitioner states since 1980, the suboptimal quality of studies would have definitely been observed and reported in the scientific literature. The reliability and integrity of diagnostic nuclear medicine would also have definitely been in question. While extravasations can occur, those that would be of potential physical harm (deterministic effect) are rare.

Because the techniques for IV administration are the same for non-radioactive drugs, many studies have been done especially for radiologic contrast agents which have demonstrated that these events are extremely low occurrences of less than a fraction of a percent.

2. Do you know of any extravasations that have resulted in harm to patients? If so and without including information that could lead to the identification of the individual, describe the circumstances, type of effect harm, and the impacts.

I have never seen or had reported an event where extravasation of a diagnostic dosage caused biological harm even though most are done by straight IV needle stick. All IV therapy administrations used an intracath connected to a 3-way stopcock arrangement to verify patency of IV connection and provide flush to the injection syringe. There was never any observation of a biological effect or a patient complaint of physical effects at administration. My personal experience includes P-32 colloid for interstitial treatment and IV administrations of P-32 sodium phosphate, Sr-89 chloride, Sm-153, and Ra-223 (Xofigo). I believe this speaks highly of the training and skill of the registered nuclear medicine technologists involved in these administrations. Two of the more recent studies looking at these events [*George S Larcos, GS, Collins, LT , Georgiou, A et al. Maladministrations in nuclear medicine: revelations from the Australian Radiation Incident Register. MJA 2014; 200: 37–40; Van der Pol, J., Voo, S., Bucerius, J. et al. Consequences of radiopharmaceutical extravasation and therapeutic interventions: a systematic review. Eur J Nucl Med Mol Imaging (2017) 44:1234–1243*] found either "no discernable or projected radiation safety consequence" or no irreparable physical harm.

3. For medical use licensees, does your facility currently monitor for radiopharmaceutical extravasation? If so, why and how do you monitor? If not, why not?

4. 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?

It will not improve if expensive equipment and novel dosimetry methodology must be employed that is beyond capability and availability of community level nuclear medicine departments. What possible specific changes can be done in the straightforward IV injection for the administration of a diagnostic radiopharmaceutical? The techniques employed are taught routinely in technology and nursing programs and used by any nuclear medicine technologist hundreds of times per year. Nothing in the petition offers any specific measures a technologist can take to prevent an extravasation or manage it after it has occurred. The fallacy of the petition is that monitoring will prevent infiltration/ extravasation when even Lucerno's own most recent study (Wong et. al.) demonstrates that it does not. The IV administration of any drug requires a medical technique and as such falls under the practice of medicine.

5. 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?

No. This petition assumes that if an extravasation occurs, the licensee must have done something wrong and all extravasations are preventable. That is completely false. The act of administering drugs to patients is the practice of medicine. The petitioner offers no evidence or specific information on how monitoring can prevent extravasations. How is improvement going to be shown if such events are rare and there is no way to tell if the cause was technique or patient condition? The NRC has no expertise in this area.

More important is how this regulatory monitoring is to be done since there are no acceptable standard methodologies known. If the NRC is going to mandate by regulation, then it must provide the procedures, acceptable equipment, and a standardized methodology on performance. A more acceptable and practical standard would be to suggest in licensing guidance that standard medical practices be assured to monitor and evaluate intravenous injection sites for signs of extravasation. This can be done by existing observation, patient inquiry, and follow-up methods and are not intrusive into the practice of medicine, expensive, time consuming, or adversely affect patient care.

Medical Event Classification and Reporting Criteria Questions

1. 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?

There are no benefits to approving this petition. No one – licensees, NRC, or patients – would benefit from this petition except the petitioner, Lucerno. The burden to licensees would be significant because methodology to quantitate extravasations are unproven and no standard exists that is recommended or adopted by a relevant radiological professional organization. Financial burden would be incurred to obtain and maintain the needed software and equipment to analyze and quantitate the information. Only very few licensees have the human resources to collect and generate the quantitative results from an infiltration and assess an absorbed dose from that result. These assessments can take considerable time (i.e., multiple days) to accomplish, which nearly all licensees cannot do.

Another added burden that would occur is resulting regulatory process that comes into play when a medical event is reported: 1) the licensee is identified publicly and immediately on reporting into the Medical Event notification center; 2) invariably an on-site inspection and enforcement is initiated; and 3) NRC has no criteria or expertise to evaluate IV administration techniques.

The reporting of medical events under §35.3045(a) were created to provide some monitoring that an administration of byproduct material was delivered in accordance with the written directive or physician's imaging protocol. This rationale does not apply to extravasation scenarios because they occur even though the administration proceeded as intended and in accordance with best practices. The NRC would need to create medical event that is contrary to its current stated purpose and redefine purpose of a medical event.

The reporting of extravasations to a federal agency would be unprecedented. No other agency – state or federal – has a requirement to report intravenous extravasations of drugs, even for highly toxic chemotherapy agents.

2. 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)?

I am prefacing this response by identifying that when I was a nuclear medicine physicist representative on the ACMUI. I chaired the subcommittee that annually reported on medical and medical nuclear material events. Accordingly, I have an intimate and detailed knowledge of NMED reports and have followed subsequent annual subcommittee reports. The following issues have been repeatedly documented over the past 15 years: medical events are underreported; NMED reports often devoid of details and causative factors; and rarely are trends found that can be useful to other licensees. Creating another medical event with a highly questionable basis will only contribute to this problem. Already, as indicated in my comments, the preponderance of information demonstrates that extravasations reporting will not identify problems or trends or useful actions to prevent these events.

All methods of identifying extravasations are post-injection, and none, including the petitioner's quality control survey meter, can determine if an extravasation was caused by patient condition or administrative technique.

Also, this question exemplifies a fundamental problem with the petition. There is nothing provided in the petition indicating what can be done to improve administration techniques or the safety practices by the licensee or the Authorized User. An erroneous implication of the petition is that nuclear medicine technologists, for whom the NRC has no specific training requirements, are performing these administrations improperly. Registered technologists undergo specific training and monitoring of their administration techniques, which are universal. Rather than create a medical event that will only be addressed at the administering person, i.e., the nuclear medicine technologist, the NRC would have much greater effect on ALARA and patient safety if it established the credentials of those that administer IV radiopharmaceuticals.

3. 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?

By definition, diagnostic agents do not elicit biological responses; they are tracers. There has been absolutely no biological harm reported for diagnostic radiopharmaceutical injections. Even for therapeutic intravenous injections, the petitioner provides no evidence of irreparable biological harm caused by the method of administration. Only making therapy radiopharmaceutical extravasations reportable does not change the fundamental problems with this petition which are it would be expensive, resource-intensive, and an adverse imposition into the practice of medicine for events that are rare.

I appreciate the opportunity to comment on NRC PRM-35-22. I strongly recommend that this petition be denied. This is a burdensome and disturbing petition put forth by a company with a vested financial interest in its adoption. All the monitoring data supporting this petition is based on their own controlled studies with their own device. The creation of a medical event category based on the information provided by single commercial company and without the corroboration of unbiased and independent medical sources would be an unconscionable mistake.

If the NRC truly believes that extravasations are still a regulatory issue, it would be much better served to address alternative measures with professional organizations such as American College of Radiology, Society of Nuclear Medicine and Molecular Imaging, and American Society of Radiation Oncology. There may be actions that are simple and effective to assess and document and manage for IV administrations suspected of being extravasated and can be implemented via regulatory guidance without creating a questionable medical event.

Sincerely,

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