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September 1, 2023

Irene Wu
U.S. Nuclear Regulatory Commission
Washington, DC 20555–0001

Dear Ms. Wu,

The OAS Executive Board (Board) appreciates the opportunity to comment on the Nuclear Regulatory Commission (NRC) proposed rule Reporting Nuclear Medicine Injection Extravasations as Medical Events as described in Docket ID NRC-2022-0218; including notifications received under STC-23-033 (Notification of Issuance of Federal Register Notice Requesting Information Regarding a Rulemaking on the Reporting of Nuclear Medicine Injection Extravasations as Medical Events) and STC-23-052 (Notice of Extension of Comment Period for Information Request Regarding Rulemaking on the Reporting of Nuclear Medicine Injection Extravasations as Medical Events).

After soliciting comments from our Agreement State partners, the Board received comments from Arkansas, Colorado, Nebraska, and Rhode Island, as well as comments from Nebraska which supported comments made by the National Institutes of Health received by the NRC. Comment letters from Arkansas, Rhode Island, and the Nebraska supported comments made by the National Institutes of Health appear to have been already submitted to the NRC as part of the public comment period and are included as attachments to this letter for completeness.

As comments to the preliminary proposed rule language, the Board has the following comments:

- The definition of 'Extravasation' is too broad. The definition should include qualifying language such as '…unexpected leakage…'. A definition of 'leakage' should be provided to not include biological processes. This definition also does not include material where a dose does not enter a blood vessel (i.e. injected completely into surrounding tissue or for a completely infiltrated needle).
- The definition of 'Medical attention' is too broad. 'Medical attention' should be limited to treatments recommended or provided by a physician where a suspected radiation injury has been diagnosed.
- The definition of 'Suspected radiation injury' is too vague, where a potential deterministic health effect could be interpreted differently by different physicians and / or different licensees, leading to an inconsistent application of the regulations.
- The proposed 10 CFR 35.42 requires licensees to develop procedures to adequately detect suspected radiation injuries that require medical attention. The proposed definition of medical attention includes techniques used to reduce the chance of an injury. It is not clear how it is possible to reduce the chance of an injury that has already occurred.

As part of Docket ID NRC-2022-0218, the NRC solicited comments on 14 questions. The comments to those questions are as follows:

1. What term should the NRC use (e.g., extravasation, infiltration) when describing the leakage of radiopharmaceuticals from a blood vessel or artery into the surrounding tissue?

> The NRC should use the term 'extravasation'; however, care should be exercised in the definition such that normal biological extravasation is not considered as part of the definition. The definition should ensure that any residual radiopharmaceutical that adheres to the injection site is not considered as a potential extravasation. The ACMUI, AAPM, or other physicians should be consulted to ensure the proposed definition is not contrary to the standard used across the medical industry.

2. What criteria should the NRC use to define "suspected radiation injury"?

> The NRC should consult with the ACMUI, AAPM, and other physicians to develop this definition. The definition should include that the suspected radiation injury is identified by a physician or other medical professional trained to identify the cause of the suspected injury and not by untrained members of the public. Additionally, the criteria for the definition should include set values to minimize the subjectivity of physician interpretation.

3. What techniques or methods should be included in the definition of "medical attention"?

> Similar to question #2, the NRC should consult with the ACMUI, AAPM, and other physicians to develop this definition. The definition should include that medical attention is initiated by a physician or other medical professional trained in identifying a suspected radiation injury and the appropriate medical attention. The definition should be crafted such that an untrained member of the public cannot be giving medical attention, nor should a patient be self-prescribing their own medical attention (for example, taking a pain reliever for a sore injection site should not be construed as medical attention from a suspected radiation injury).

4. What steps could the licensee take to minimize the chance of a radiopharmaceutical extravasation occurring?

> Training, including refresher training or recertification training required by various regulatory or certifying bodies for medical treatments, should be sufficient to address and prevent any extravasation from occurring regardless of whether the pharmaceutical contains a radioactive component or not. Licensees could utilize IV needles for administering radiopharmaceuticals instead of directly injecting those materials as an individual administering radioactive materials could flush an IV and verify the patency of an IV prior to administration which could help minimize the chance of an extravasation.

5. What steps should the licensee take when an extravasation is suspected or discovered?

> A licensee should take overall patient health into consideration for any extravasation. Guidance should be developed to ensure a consistent approach is taken by all licensees across the National Materials Program.

6. What techniques, technologies, or procedures (e.g., post-treatment imaging, visual observation, patient feedback) should be used to help identify an extravasation during or immediately after a radiopharmaceutical injection?

Post-treatment imaging and visual observation could be used to help identify an extravasation; however, it should be recognized that radiopharmaceuticals that remain at an injection site may or may not constitute an extravasation or medical event. Patient feedback will likely be unreliable as effects may not be immediately recognized by a patient, or may not be immediately evident.

7. What techniques, technologies, or procedures (e.g., post-treatment imaging, survey measurement) should be used to better characterize an extravasation after radiopharmaceutical treatment?

Post-treatment imaging, survey measurement, and consultation with an authorized user should be used to better characterize an extravasation.

8. What information should licensees provide to nuclear medicine patients on how to identify an extravasation and how to follow up with their physician if they suspect a radiation injury?

Patients could be provided with a timeline of physical symptoms that aligns with the definition of "suspected radiation injury" including contact information for the authorized user involved with the patient treatment.

9. When should a reportable extravasation be counted as "discovered" for the purposes of notification (e.g., when medical attention is administered, when the physician identifies that the injury is from radiation)?

The "discovered" time should be after the "suspected radiation injury" is identified by an authorized user or authorized medical physicist.

10. The NRC requires that licensees notify the referring physician and the individual who is the subject of a medical event no later than 24 hours after discovery of the medical event. When should licensees be required to provide notification of an extravasation medical event to the referring physician and the individual?

There should be no change to the reporting requirement.

11. Who (e.g., patient's primary physician, authorized user, nuclear medicine technician) should be able to identify an extravasation that could result in a "suspected radiation injury"?

A "suspected radiation injury" should be identified by a physician or by an authorized medical physicist.

12. What topics should the NRC include in guidance to assist licensees to accurately identify, characterize, and report extravasation events in a timely manner?

Guidance should be created that includes the topics identified in the question itself. Guidance should be accessible for all licensees that use radiopharmaceuticals and should also include general instructions to patients who may believe they have a "suspected radiation injury". Examples of acceptable procedures required by draft 10 CFR 35.42, or a description of what items should be addressed in those procedures, would be helpful for licensees.

13. What regulatory actions could help ensure that extravasations in patients affected by healthcare inequities are accurately assessed and reported?

Any regulatory actions should ensure that patients of disproportionally impacted communities, as well as patients in rural settings, have the assurance that medical treatments involving radiopharmaceuticals are conducted in a safe manner. Requiring rural facilities to purchase

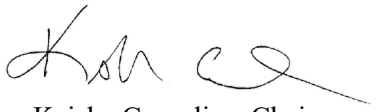
additional equipment may prevent those facilities from offering nuclear medicine tests in the future, thereby increasing healthcare inequities in those populations.

14. Are vascular access tools and other technologies (e.g., ultrasound guided vein finders) likely to reduce the potential for an extravasation in all patients, particularly in patients of color?

The ACMUI, AAPM, and other physicians should be consulted for this item.

Once again, the Board appreciates this opportunity to comment. We are available should you have any questions or need clarifications to our responses.

Sincerely,



Keisha Cornelius, Chair
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July 3, 2023

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

Re: Comments on extravasations as medical events – preliminary proposed rule language (Docket ID NRC-2022-0218)

Dear Mr. DiMarco:

Thank you for the opportunity to comment on the extravasations as medical events preliminary proposed rule language relating to Docket ID NRC-2022-0218. Please consider the following comments:

DEFINITIONS

Questions #1 - #3

However "extravasation," "suspected radiation injury," and "medical attention" are defined, criteria in the language must be able to largely tease out the potentially harmful administrations from those that are not. A patient or human research subject should not be worried unnecessarily, nor should the licensee be burdened with no programmatic benefit.

Clear guidance documents must supplement the rule language in order to instruct technologists how to implement any new reporting requirements. The Commission should be realistic as to who can appropriately make the required determinations via their training, experience, availability, etc. and what resources (additional training, equipment, etc.) new reporting requirements will necessitate.

Federal Register Notices of the proposed and final rules must also be very clear, with examples, etc., for distant future use, so as to appropriately interpret past intentions.

PROCEDURES

Question #4

Any administration at a greater risk of causing radiation injury should be bound by appropriate procedures, reviewed by the governing body prior to license issuance, to help prevent such an injury. Procedures addressing possible *prevention* in regard to an extravasation seem to be missing from the

preliminary proposed rule, unless the extravasation was due to an administration requiring a written directive. § 35.41 requires implementing of written directive procedures "to provide high confidence that each administration is in accordance with the written directive." This wording includes preemptive actions supporting correct delivery of the administration requiring the written directive. An extravasation might cause a radiation injury but might not be as a result of an administration requiring a written directive. The new § 35.42 only mentions after the fact detection and reporting of the extravasation.

Question #5

Process-improving procedures can be a result of reporting an event.

Questions #6 and #7

Techniques, technologies, and procedures used to help identify an extravasation should be flexible due to facility capabilities (no imaging on-site or other equipment limitation) and patient/human research subject differences (extravasations not always visible or different patient/human research subject tolerance). Procedures could be reviewed during the licensing process in order to determine if the items implemented for extravasation identification purposes meet the "high confidence" requirement stated in the new § 35.42. Examples of what actions could provide "high confidence" would need to be explained in updated licensing guidance and memorialized in the Federal Register proposed and final rule notices.

Question #9

Based on the current preliminary proposed rule definitions, an "extravasation that requires medical attention for a suspected radiation injury" cannot be determined until the "suspected radiation injury" portion of the "medical attention" definition has been determined first.

Question #10

To prevent confusion, reporting specifics in § 35.3045 should be the same for any incident determined to be a "medical event."

Question #11

An Authorized User (AU) authorized for the type of use involved in the extravasation should ultimately be the individual who identifies an extravasation that could result in a "suspected radiation injury." Work experience required of the AU in §§ 35.190(c)(1)(ii), 35.290(c)(1)(ii), 35.390(b)(1)(ii), 35.396(b)(2), and perhaps other sections should include "Identifying a medical event, once it has occurred, involving the use of byproduct material."

A nuclear medicine technologist under supervision of the AU can use byproduct material pursuant to § 35.27. "Extravasation procedures" should be added to the list of items supervised individuals must be instructed in and to the list of instruction topics the supervised individuals must follow (§ 35.27(a)(1) and (a)(2), respectively).

The licensee's procedures developed pursuant to the new § 35.42 should specify the roles of individuals (e.g., nuclear medicine technologist, Authorized User, Authorized Medical Physicist, etc.) pertaining to possible extravasations. Updated licensing guidance should give examples of identification scenarios allowed under the regulations.

Question #12

Topics that the Commission should address in guidance are discussed in Department responses to Questions 1-3, 6-7, and 11, and in the response below concerning the preliminary proposed rule language for the new § 35.42(a).

PRELIMINARY PROPOSED RULE LANGUAGE

New 10 CFR 35.42(a)

"Timely manner" could be seen as nebulous and hard to inspect against. Perhaps updated licensing guidance and the Federal Register Notices could give examples of what would be considered as being done in a "timely manner." Is the intent of the use of "timely manner" to prescribe when *detection* of the extravasation should occur? Should the provision therefore say "…will be detected in a timely manner and reported in accordance with § 35.3045."? Otherwise, it appears two time intervals for the reporting portion are ambiguously listed…timely and no later than the next calendar day after discovery of the medical event (§ 35.3045(c)).

The Department assumes that administrations involving a written directive and where an extravasation can occur must follow both § 35.41 and the new § 35.42, since procedures developed for prevention of the event, i.e., that the administration is in accordance with the written directive, would only be captured under § 35.41. For the sake of clarity, the new § 35.42(a) could say "In addition to § 35.41, as applicable, for any administration in which an extravasation can occur, the licensee must…"

We appreciate the opportunity to comment on this preliminary proposed rule language. If you have any questions, please contact us at (501) 661-2301.

Sincerely,

Angela Minden

Angela Minden, BS, CNMT
Technical Activities Health Physicist
Radiation Control Section
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cc: Bernard Bevill, Section Chief

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22 August 2023

Adelaide Giantelli, Chief [via e-mail: [Adeliade.Giantelli@nrc.gov]
State Agreement and Liaison Programs Branch
Division of Materials Safety, Security, State, and Tribal Programs
Office of Nuclear Material Safety and Safeguards
U.S. Nuclear Regulatory Commission
Washington, DC 20555-0001

RE: Notification of Issuance of Federal Register Notice Requesting Information Regarding a Rulemaking on The Reporting of Nuclear Medicine Injection Extravasations as Medical Events (STC-23-033).

Notice of Extension of Comment Period for Information Request Regarding Rulemaking on The Reporting of Nuclear Medicine Injection Extravasations as Medical Events (STC-23-052)

Dear Ms. Giantelli:

The Rhode Island Agreement State Program has received and reviewed the Commission's Federal Register Notice Requesting Information Regarding a *Rulemaking on The Reporting of Nuclear Medicine Injection Extravasations as Medical Events* (STC-23-033), Notice of *Extension of Comment Period for Information Request Regarding Rulemaking on The Reporting of Nuclear Medicine Injection Extravasations as Medical Events* (Stc-23-052). the Commission's preliminary proposed rule language for reporting nuclear medicine extravasations as medical events [NRC-2022-0218; RIN 3150-AK91], and relevant supporting documents on the Commission's rulemaking website. We appreciate the opportunity to comment on these documents.

Our first concern is the PRM itself. We consider the original petition to the NRC to be an unethical, alarmist attempt to make money off unavoidable medical exposure to radiation and feel that the petition process was abused by a profit-seeking entity and in so doing, cost the American public millions of dollars in NMP staff productivity debating their unreasonable requirement to detect the extent of extravasations.

Our second concern is the lack of specificity as to when a nuclear medicine extravasation must be reported as a medical event. The proposed criterion for reporting a medical event appears to be a *suspected radiation injury* which is further defined as *a potential or observable deterministic health effect for to the area around an injection site that can be attributed to radiation*. This is subjective at best and there will probably be as many definitions as there are nuclear medicine licensees. The majority of the criteria in the current regulations which deal with reporting a medical event are definitive and linked to a specific exposure in one way or another. The original SECY brief on this topic included an exposure level which was the threshold for *suspected radiation injury*. However, this value was not included in the proposed regulatory text. We ask that NRC revisit this issue and come out with some definitive exposure that meets the *suspected radiation injury* criteria. Otherwise, we are likely to have a situation where an identical situation occurs at two facilities and reporting is inconsistent because each facility has used a different basis for determining what constitutes a *suspected radiation injury*.

A quick review of the comments already submitted to the rulemaking docket would appear to indicate that there is no consensus as to the frequency of extravasation events or at what point does an exposure from an extravasation event rise to the rigorous standard set for currently reporting medical events. Until these two basic issues are resolved, we strongly recommend that NRC withdraw this proposed rule from any future consideration.

We have no further specific comments to offer at this time.

If you have any questions regarding this letter, please contact the undersigned at (401) 222-4249 or via e-mail (alexander.hamm@health.ri.gov).

Sincerely,

Alexander Hamm
Supervising Radiological Health Specialist
Radiation Control Program
Center for Health Facilities Regulation

cc: Irene Wu [via e-mail: Irene.Wu@nrc.gov]
Phillip Peterson, OAS Director of Rulemaking [via e-mail: phillip.peterson@state.co.us]

From: Ribaudo, Cathy (NIH/OD/ORS) [E]
To: RulemakingComments Resource
Subject: [External_Sender] Comments on NRC-2022-0218
Date: Wednesday, August 16, 2023 10:38:59 AM
Attachments: Comments on Reporting Extravasations at Med Events.pdf

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Good morning; this attached comment is to be directed to Irene Wu and Daniel DiMarco. This comment is being submitted on behalf of the National Institutes of Health, Bethesda, MD.
Thank you for your attention,
Cathy

Catherine Ribaudo
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pronouns: she/her (why?)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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Bethesda, Maryland 20892

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August 15, 2023

Secretary,
U.S. Nuclear Regulatory Commission
Washington DC 20555-0001
ATTN: Rulemakings and Adjudications Staff

Dear Sir/Madam,

This is a submittal of comments in response to the NRC public request regarding the proposed rulemaking revision to 10 CFR Part 35 "Reporting Nuclear Medicine Injection Extravasations as Medical Events" (Docket ID: NRC-2022-0218).

At the May 2023 meeting of the Advisory Committee on the Medical Use of Isotopes (ACMUI), which NIH attended, several licensees shared their opposition to this proposed reporting policy. A frequently expressed sentiment was that extravasations are common occurrences in the application of contrast agents and pharmaceuticals and do not lead to patient harm, nor to an increase in repeat radiopharmaceutical administrations. NIH agrees with those in opposition to the proposed reporting policy as written.

The proposed reporting policy would require licensees to report, as a medical event, the administration of byproduct material that results in an extravasation requiring medical attention for a suspected radiation injury. "Suspected radiation injury" means a potential for observable deterministic health effect to the area around an injection site that can be attributed to radiation. "Medical attention" means any technique(s) used to reduce the chance, severity, or symptoms of a suspected radiation injury.

Therefore, the simple elevation of an arm, massaging the injection site, or use of a cooling or heating pad to minimize the local dose could lead to concern that the extravasation is requiring medical attention and qualify as a reportable medical event.

It would be preferable for the NRC to adopt the medical event reporting criteria already established in 10 CFR 35.3045(a) and (b) to define extravasation risk. This would allow for the prompt reporting of radiation safety-significant extravasations from high energy radiopharmaceuticals and curtail the reporting of minor and common extravasation events from low dose radiotracers that do not contribute to an increased radiation risk. The vast majority of diagnostic nuclear medicine administrations would not meet reporting criteria if an extravasation occurred, and thus the focus could, and should, be on therapeutic administrations where activities or energies are more potent.

NIH would be in favor of reporting extravasations involving therapeutic radiopharmaceuticals. Nonetheless, clear guidance as to the applicability of a medical event reporting requirement should cover extravasations no differently than other events covered in 10 CFR 35.3045(a) and (b).

I hope the NRC finds these comments useful. If you have any questions or need additional clarification on our submittal, please contact me at 301-594-1303 or via e-mail at cribaudo@nih.gov.

Catherine Ribaudo
NIH Radiation Safety Officer

cc: Dr. Liza Lindenberg, Chair, RSC, NIH
Dr. Nina Schor, Deputy Director for Intramural Research, NIH