American College of Radiology

September 1, 2023

Submitted electronically via Regulations.gov

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

Re: (Docket ID NRC-2022-0218; 88 FR 24130) Reporting Nuclear Medicine Injection Extravasations as Medical Events—Preliminary Proposed Rule Language and Notice of Availability; Comments of the American College of Radiology

The American College of Radiology (ACR)—a professional association representing over 41,000 diagnostic radiologists, interventional radiologists, nuclear medicine physicians, radiation oncologists, and medical physicists—appreciates the opportunity to comment on the April 19, 2023, notice of availability and preliminary proposed rule language from the U.S. Nuclear Regulatory Commission (NRC) regarding "Reporting Nuclear Medicine Injection Extravasations as Medical Events" (Docket ID NRC-2022-0218).

Background

On May 18, 2020, Lucerno Dynamics, LLC, filed a petition for rulemaking (PRM-35-22) urging NRC to require certain nuclear medicine extravasations to be reported by healthcare providers as "Medical Events (MEs)" based on unique measurements and controversial dose estimations. If approved, the petition would have impacted up to 20 million nuclear medicine procedures annually with new tool/protocol mandates specific to NRC compliance and outside relevant medical standards of care and radionuclide dosimetry. The petitioning company sells a specialized proprietary system of measurement devices and dosimetry software referenced throughout the public docket.

PRM-35-22 was published for comment on September 15, 2020, and received nationwide opposition and criticism from medical and scientific experts unaffiliated with the petitioner's campaign. In December 2022, the NRC Commissioners voted unanimously to implement ME reporting of harms instead of mandating acquisitions or use of third-party tools. NRC requested stakeholder perspectives on key questions and draft language on April 19, 2023, to inform the agency's future Notice of Proposed Rulemaking (NPRM) planned for 2024.

General Comments

The current, long-standing NRC enforcement policy on extravasation has adequately protected public health and safety for decades without issue or justification for a change in approach. However, the ACR generally supports the NRC Commissioners' unanimous, bipartisan decision to close the PRM-35-22 docket and mandate ME reporting of any hypothetical extravasation occurrence that "*requires medical attention for suspected radiation injury*" (SRM-SECY-22-0043). Commonsense, risk-informed regulatory implementation focused on deterministic radiation harm is key to avoiding unintended consequences for patients and providers.

The ACR recommends that NRC staff partner with healthcare regulatory and research agencies, providers, accreditation bodies, pharmaceutical manufacturers, and national medical/scientific professional associations to avoid conflicts with routine safety practices, institutional quality assurance (QA) programs, drug/device labeling, and medical standards of care.

Extravasation and Practice of Medicine

Extravasation—meaning leakage of blood/lymph/fluid, or physiologic/pathologic movement of cells, from the blood vessel into surrounding soft tissue—is a potential complication of any intravascular administration with any drug or liquid [1]. While all liquids can and do extravasate, not all extravasated liquids share the same injury risk profile. Extravasation injuries are typically caused only by either large fluid volume leakages or by soft tissue contact with vesicant agents (e.g., nonradioactive chemotherapy, or other agents that can blister or otherwise

damage tissue upon contact) [2]. Neither scenario is realistically applicable to small volume injections of low dose radiopharmaceuticals, which when extravasated are typically reabsorbed by the body's systems spontaneously, often without noticeably adversely impacting the patient or preventing the success of the nuclear medicine imaging or therapy procedure.

Venous access in the routine practice of medicine intrinsically requires consideration of various risks and benefits. Available clinical methods for reducing extravasation frequency (such as use of central venous catheters, surgically implanted ports, or specific large catheter types/bores, etc.) introduce additional risks and consequences for patients that must also be weighed in this calculus. These risks can include bleeding, infection, and structural concerns with large-bore access as well as carotid artery puncture, subclavian artery puncture, pneumothorax, hematoma formation, hemothorax, and other complications with central venous access. Generally, it is standard practice to use the access method with the lowest risk profile appropriate for the patient, clinical context, and drugs/media.

In diagnostic radiology, interventional radiology, nuclear medicine, and radiation oncology, extravasation management is a critical component of vascular access training, procedures, and policies. These departments routinely administer larger fluid volumes of higher risk non-radioactive contrast agents or other drugs/liquids. Unlike asymptomatic radiopharmaceutical extravasation, which typically resolves rapidly without intervention, severe extravasations of non-radioactive contrast agents and other large fluid volume materials can result in sentinel event-level injury such as acute compartment syndrome [2]. Yet, despite the greater risk, focused large-scale, nationwide practice improvement efforts to reduce the frequency, severity, and distribution of symptomatic extravasation with non-radioactive contrast media have been unsuccessful [3].

Definitions

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

Clinical and scientific understandings of "extravasation" and "infiltration" terms can vary by context. Neither term is defined elsewhere in the Code of Federal Regulations for healthcare regulatory purposes. However, the U.S. Department of Health and Human Services (HHS) National Institutes of Health (NIH) National Cancer Institute (NCI) currently defines "*extravasation*" as:

> *"The leakage of blood, lymph, or other fluid, such as an anticancer drug, from a blood vessel or tube into the tissue around it. It is also used to describe the movement of cells out of a blood vessel into tissue during inflammation or metastasis (the spread of cancer)."* [1]

NRC could limit the "extravasation/infiltration" definition in §35.2 to §35.300 therapeutic uses, as §35.3045(a)(3) would realistically exclude any foreseeable effects of extravasated §35.200 material. For example, the defined term in §35.2 could be titled, "*extravasation of unsealed byproduct material for which a written directive is required*."

NRC Question 2: What criteria should the NRC use to define "suspected radiation injury"?
NRC Question 3: What techniques or methods should be included in the definition of "medical attention"?

NRC Questions 2 and 3 address co-dependent terminology for the proposed §35.3045(a)(3) "extravasation ME" category, and therefore the below response is applicable to both questions.

The NIH-NCI Common Terminology Criteria for Adverse Events (CTCAE, currently Version 5.0) is a descriptive HHS terminology standard for adverse event reporting. The CTCAE uses a precise severity-based grading scale for each adverse event in every organ system and body part. The NIH-NCI standard of Grade 3 and Grade 4 describes when an adverse event is medically significant.

> *"Grade refers to the severity of the AE. The CTCAE displays Grades 1 through 5 with unique clinical descriptions of severity for each AE based on this general guideline:*
> ***Grade 1*** *Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.*
> ***Grade 2*** *Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental activities of daily living.*

Grade 3 *Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living.*
Grade 4 *Life-threatening consequences; urgent intervention indicated.*
Grade 5 *Death related to AE.*
A Semi-colon indicates 'or' within the description of the grade." [4]

The Commissioners' directive in SRM-SECY-22-0043 mandated NRC ME reporting when extravasation "requires medical attention for suspected radiation injury." Corresponding NRC definitions should therefore be based on when intervention is necessary following medical assessment. This must exclude alleviative care provided by technologist or nursing personnel for various minor CTCAE Grade 1 and 2 reactions to allergens, irritants, or punctures that present with redness, swelling, pain, or sensitivities. Including such transient symptoms and clinically insignificant incidents managed primarily through observation, self-care, or local/non-invasive assistance would result in misidentified or low-quality ME reports for which the reporting burden outweighs the NRC's regulatory data collection benefit.

Therefore, "suspected radiation injury" could be defined in §35.2 as:

> "*Suspected radiation injury* means an adverse event assessed by an Authorized User, Authorized User-eligible, or Authorized User-designated physician to be: (a) caused by radiation from extravasated material, and (b) meeting the corresponding CTCAE Grade 3 or Grade 4 standard." Or,
>
> "*Suspected radiation injury* means a severe or medically significant adverse event assessed by an Authorized User, Authorized User-eligible, or Authorized User-designated physician to be attributed to radiation."

"Medical attention" could be defined in §35.2 as:

> "*Medical attention* means a treatment, procedure, or other action taken to prevent or treat disease. Medical attention is deemed 'required' pursuant to 10 CFR 35.3045(a)(3) when necessary to treat a suspected radiation injury assessed by an Authorized User, Authorized User-eligible, or Authorized User-designated physician to be severe and medically significant, disabling, or limiting self-care activities of daily living."

Procedures

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

Standard medical practice is to use the lowest total risk vascular access device/procedure feasible for the patient and clinical objective, informed by injection safety standards, patient needs, product labeling/insert instructions, drug risk profiles, clinical capabilities, procedure guidelines, etc. Institutional/departmental policies address issues such as personnel training, appropriate injection site selection, medical device use (catheter type, length, caliber), injection site monitoring, evaluation, and follow-up. [2,7,9]

The potential for extravasation is among numerous considerations weighed in risk/benefit-based decision-making with respect to vascular access procedures and policies. While all liquids can and do extravasate, not all liquids and volumes share the same injury risk profile when extravasated. Certain approaches used for high safety risk liquids and large fluid volumes are not universally applicable for all patients, settings, and liquids. For example, central venous access would invariably reduce the chance for clinically significant extravasation compared to peripheral venous access and direct injection, but at the cost of introducing the risk of pneumothorax, hemothorax, infection, or other potential mechanical complications of the vascular access procedure. NRC regulations and guidance must not unduly influence patient care toward more complex/higher risk procedures, techniques, and devices.

As defined by NRC policy as well as the preliminary §35.2 definition, extravasation occurrence does not necessitate or indicate erroneous intravenous administration by the operator. The potential for extravasation occurrence of any drug/liquid is influenced by many variables, such as:

- Demographics, such as weight, early pediatric or advanced age groups, unconscious/altered conscious, gender (women are shown to have mildly increased potential), vascular size, and fragility.
- Medical conditions/history such as altered circulation (as with atherosclerotic peripheral vascular disease, diabetic vascular disease, Raynaud's disease, venous thrombosis or insufficiency), prior radiation therapy or surgery (e.g., axillary lymph node dissection or saphenous vein graft harvesting) in the limb to be injected.
- Any movement disorder or musculo-skeletal or other disorder increasing the patients' inability to remain still during instillation.
- Catheter type and bore – Occurrence is more frequent with smaller bore catheters than larger bore.
- Osmolality and viscosity of administered material.
- Access site – hand, wrist, foot, and ankle sites are shown to result in greater extravasation frequency. [2]

Extravasation minimization is appropriately addressed by institutional vascular access procedures and policies. NRC could potentially require licensees to maintain relevant written procedures outlining their 35.3045(a)(3) post-assessment ME reporting process, but NRC should not influence the clinical content of vascular access procedures and policies.

NRC Question 5: What steps should the licensee take when an extravasation is suspected or discovered?
For *non-clinically significant or asymptomatic extravasation* of a radiopharmaceutical, the patient consequence is typically limited to variable impacts on speed of imaging/therapy site delivery and procedure completion. The traces of partially extravasated dose would be absorbed in the vascular or lymphatic system and delivered to its imaging or therapy target. Similar effects on uptake speed could also occur due to altered circulation, impaired kidney function, venous stasis, or other reasons unrelated to extravasation. If the patient is asymptomatic or has only mild symptoms, evaluation and any requisite follow-up is usually sufficient [2].

For *apparent or symptomatic extravasation*, the provider would examine the patient. Depending on the extravasated fluid volumes and drug/media, physical examination could include assessment of tenderness, swelling, erythema, paresthesia, active and passive range of finger motion, and perfusion. Certain patients might also be held for an appropriate interval for observation and discharged with situationally appropriate instructions. Depending on severity (note: more typical to large volume non-radioactive contrast media), follow-up could be planned in appropriate intervals. It is standard medical practice for any symptomatic extravasation to be documented in the medical record, even if injury does not result. Provider policies often include imaging the injection site to aid assessment if substantial extravasation is suspected. If a diagnostic quality imaging study were impeded, this would be evident to the reading physician and documented in the medical record/radiology report. In extremely rare cases in which diagnostic quality was not achieved, the study may be repeated, as it would be for any impediment. [2,8]

NRC Question 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?
General approaches for apparent or symptomatic extravasation are provided in the above response to NRC Question #5.

Importantly, all such issues would be covered by existing vascular access procedures and policies within NRC-licensed healthcare facilities. §35.200 and §35.300 licensees routinely use much higher extravasation injury risk drugs and other non-radioactive media and have applicable expertise in extravasation management.

NRC Question 7: What techniques, technologies, or procedures (e.g., post-treatment imaging, survey measurement) should be used to better characterize an extravasation after radiopharmaceutical treatment?
Characterization of severity for §35.3045(a)(3) purposes should be based on AU, AU-eligible, or AU-designated physician qualitative assessment to determine if there is a radiation-attributable CTCAE Grade 3 or Grade 4 event. This assessment could use any combination of inputs pursuant to institutional policies, including medical record documentation, physician examination, injection site imaging (if performed), QA tools [10], other provider feedback, patient feedback, etc. Valid characterization approaches may vary depending on patient needs, drug risk, clinical setting, etc. Importantly, severity characterization is intrinsic to extravasation management and QA within

licensed facilities, and no specific methodology should be promoted by NRC regulation or guidance beyond ensuring that licensees have written documentation compliant with §35.42 and §35.2042.

NRC Question 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?
Pursuant to the directive in SRM-SECY-22-0043, the patient must not be burdened with licensees' NRC compliance obligations or be expected to have special regulatory knowledge. Rather, the determination of whether an extravasation meets the criteria of §35.3045(a)(3) should be via the AU, AU-eligible, or AU-designated physician's qualitative assessment, which would dictate subsequent licensee reporting to NRC. Medical assessment of severity is a routine part of extravasation management; therefore, this approach would not add NRC-unique processes or burdens for the patient.

Clinically apparent or symptomatic extravasation initiates policies and procedures for observation, evaluation/examination, patient instructions, follow-up, risk management/intervention, etc. For higher risk administrations (i.e., larger volume/higher toxicity non-radioactive contrast agents) the standard practice is for discharged outpatients to be given instructions concerning where to seek additional medical care and what to look out for should the symptoms worsen [2, 8].

Bear in mind that patients receiving nuclear medicine, nuclear radiology, interventional radiology, and radiation oncology services are commonly administered drugs/media of greater extravasation concern during or around the same episode of care (for example, with certain hybrid imaging or cancer therapies). It is critical for safety and clarity that all patient instructions on extravasation in general are pertinent and appropriate, understandable by the individual patient and/or caregiver, and seamlessly integrated into the overall instructions provided to the patient and caregiver.

NRC Question 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)?
When the AU, AU-eligible, or AU-designated physician professionally determines following completion of their assessment that a CTCAE Grade 3 or Grade 4 injury is attributable to radiation from an extravasation, it should count as "discovered" for initiating existing §35.3045(c) through (g) reporting and notification requirements.

Importantly, the discovery and reporting process for any 35.3045(a)(3) NRC ME is exclusively a regulatory compliance issue that does not alter the timing of patient care activities or healthcare communications with the patient.

NRC Question 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?
Current requirements in §35.3045(e) for notifying referring physicians/patients of the NRC filing could readily be applied to §35.3045(a)(3) MEs. However, in general, the ACR supports more administrative flexibility across the ME reporting paradigm that corresponds to NRC's use of the data being collected. Immediate NRC administrative deadlines in busy clinical environments should be reserved for ongoing threats to public health and safety where urgent NRC action is needed (e.g., to investigate sources missing in shipments, major material spills within the facility, and to collaborate with FDA/state agencies to identify defective drug/device products).

Importantly, ME reporting and notification regulations at §35.3045(c) through (g) describe an added layer of NRC-specific administrative activity that is separate and distinct from health information sharing. Per NRC's prior justifications in ME-related rulemakings, the exclusive purpose of §35.3045(e) is to formally notify recipients that the ME report in question was filed with a government agency. These regulatory notifications do not have a clinical purpose and do not change adverse event management, medical record documentation, or routine physician-patient communications. [11]

NRC Question 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"?

The ME identification/discovery process described in NRC Question 11 should be simple, straightforward, and generally aligned with licensees' existing ME-related processes. An AU, AU-eligible, or AU-designated physician must assess whether the extravasation requires medical attention for suspected radiation injury. This assessment could optionally be informed by various inputs, including information from non-AU/non-AU-eligible providers treating the patient at any time in the future. The AU has supervisory responsibilities for medical uses of byproduct material within the NRC-licensed facility, and therefore is the appropriate authority for §35.3045(a)(3) discovery.

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

NRC could require written documentation in §35.42 and §35.2042 for the process of §35.3045(a)(3) compliance. Generally, all steps up to and including the severity assessment would be covered by existing procedures and policies within the facility. NRC guidance should avoid all clinical content (e.g., vascular access procedures and devices), instead focusing broadly on the post-assessment components of the licensee reporting process. The NRC could also make available in its Medical Licensee Toolkit links to the NIH-NCI CTCAE standards for Grade 3 and Grade 4 adverse event assessment, which could guide AU, AU-eligible, or AU-designated physician assessments of reportability.

Healthcare Inequities

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

The ACR is the convening organization of the Radiology Health Equity Coalition (https://www.radhealthequity.org/), which is a network of patient-focused radiology societies focused on collecting, assessing, and disseminating resources and best practices, advocating for and connecting with patients and community members, and collaborating on programs and services to improve access and utilization of preventative and diagnostic imaging.

To prevent negative impacts on health equity of future NRC ME requirements, the ACR urges the agency to avoid any regulatory language or guidance content that would promote acquisitions of proprietary devices, software application subscriptions, or non-medically standard dose-estimation methodologies of unclear efficacy for underserved patient populations and diverse clinical settings. Any unique dose-estimate-based approach, including an NRC-devised dosimetry model, would likely have the following unintended negative consequences on health equity, particularly impacting small/rural §35.200-licensed facilities and their patients:

- Added out-of-pocket, uninsurable costs for patients, including Medicaid beneficiaries.
- Any necessity for proprietary tools and/or hiring and/or contracting with additional onsite FTE medical physicists may be infeasible for many small/rural community hospitals, imaging or therapy centers, and mobile imaging units that serve underserved patient populations, resulting in reduced patient access to essential diagnostic nuclear medicine or therapeutic radiation care.
- Real-world examples of past drug and device shortages (e.g., iodinated contrast, Mo-99, personal protective equipment) have demonstrated that medical product supply chain dependencies and resultant insecurities can lead to restricted access and triage in community hospitals, disproportionately impacting services available to underserved populations.
- Some patients may be unwilling or medically unable (i.e., due to allergies, skin trauma, or other contraindications) to have measurement sensors or other hardware adhered to their skin, as medical adhesives result in hundreds of patient-reported injuries each year per FDA Medical Device Reporting [5].
- By definition, Class I, premarket notification-exempt, "FDA listed" medical devices do not require a premarket notification application and the stringency of FDA testing and clearance/approval before such devices can be legally marketed in the U.S. This adds to potential uncertainties regarding generalizable use of unique tool-based methodologies with diverse patient populations, in disparate types of clinical settings, and with all intravenous radiopharmaceuticals [6].

NRC Question 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 ACR refers to NRC Question 4 and notes that providers currently factor available techniques and tools into risk/benefit decisions regarding vascular access procedures and policies.

With respect to the specific clinical technique in NRC Question 14, prior research with non-radioactive CT contrast media suggests increased extravasation frequency in patients in whom deep brachial intravenous access is achieved under ultrasound guidance, which is a technique most often used in emergency departments. This discrepancy may be because ultrasound-guided access is implemented in more difficult venous access situations more common to the ED. [2]

Cumulative Effects of Regulation

NRC CER Question 1: Given current or projected Cumulative Effects of Regulation (CER) challenges, how should the NRC provide sufficient time to implement the new proposed requirements, including changes to programs and procedures?

CER impacts can be minimized, though not eliminated, by focusing on standard medical significance (i.e., NIH-NCI CTCAE Grade 3 and Grade 4) and leveraging qualitative assessment of the AU, AU-eligible, or AU-designated physician to determine reportability. Regulation and guidance should avoid mandating measurement device acquisitions, employees/resources, or new patient and provider burdens for demonstrating compliance. Institutional policies and procedures currently cover most issues under consideration, and therefore NRC should appropriately rely upon existing clinical approaches and AU expertise during §35.3045(a)(3) implementation to avoid undue burdens for patients and providers.

NRC CER Question 2: If CER challenges currently exist or are expected, what should be done to address them?

NRC should preempt anticipated CER challenges by appropriately defining "*extravasations requiring medical attention for suspected radiation injury*" in a manner consistent with NIH-NCI CTCAE Grade 3 and 4 standards, as well as ensuring uniform Agreement State compatibility.

Specifically, NRC should state in the rule preamble that AU, AU-eligible, or AU-designated physician qualitative assessment is necessary for §35.3045(a)(3)-compatible regulations to secure the essential objective of §35.3045, "*to maintain a consistent national program for reporting MEs*." Per a 2018 NRC final rule, "*a consistent national program for reporting MEs allows the NRC to identify trends or patterns, identify generic issues or concerns, recognize inadequacies or unreliability of specific equipment or procedures, and determine why an event occurred and whether any actions are necessary to improve the effectiveness of NRC and Agreement State regulatory programs*" [12]. Agreement States must not mandate unique dose-estimate-based reporting methods, or any other third-party tools, processes, or methods that would create inconsistencies in state-to-state enforcement of §35.3045(a)(3) and the resultant ME data maintained in NRC's Nuclear Material Events Database (NMED).

NRC CER Question 3: What other (NRC or other agency) regulatory actions (e.g., orders, generic communications, license amendment requests, inspection findings of a generic nature) influence the implementation of the proposed rule's requirements?

In general, any rulemaking, sub-regulatory guidance, information notice, or communication to licensees or state programs could have effects on implementation and enforcement of SRM-SECY-22-0043 that add to CER concerns for licensees and regulators. The ACR is concerned that NRC guidance including a voluntary dose-estimation model could be misunderstood by individual regional or state investigators as a requirement, or even misrepresented as such by commercial interests. Enforcement inconsistencies would result in low-quality NMED data incompatible with Paperwork Reduction Act (PRA) principles, preventing achievement of the essential objective of §35.3045.

NRC CER Question 4: What are the unintended consequences, and how should they be addressed?

NRC could minimize most unintended negative consequences via:

- Implementing appropriate regulatory definitions for "extravasation," "(required) medical attention," and "suspected radiation injury" that are aligned with NIH-NCI CTCAE Grade 3 and Grade 4, the standard for medical significance requiring intervention.
- Avoiding rules or guidance describing clinical vascular access procedures and policies, including extravasation management, which could influence risk/benefit medical decision-making.
- Ensuring Agreement State compatibility with the essential objective of §35.3045 by disallowing incompatible state regulations that require dose-estimate methods or third-party tools for reportability determinations.

- Avoiding the previously mentioned negative impacts on healthcare equity of requiring third-party product acquisitions or novel methodologies that have not been stringently tested/validated by regulators with all patient populations, clinical settings, and radiopharmaceuticals.

NRC's April 2023 "preliminary proposed rule language" for §35.2 definitions included minor reactions (i.e., redness, swelling) and alleviative, noninvasive assistance provided by supervised personnel (i.e., cold/warm compress, limb elevation). Such reactions are relatively immediate, post-instillation and likely not due to radiation causes. This approach would likely lead to the following unintended consequences due to CER:

- Prevalent misidentification of minor, transient reactions of any kind as §35.3045(a)(3) MEs. This would be inclusive of allergic reactions, puncture reactions, irritation, hypersensitivities, extravasation of non-radioactive drugs/media provided to the same patient during the same episode of care, etc.
- Medically unjustifiable escalation of concern with byproduct material extravasations that may influence vascular access procedures and distract from higher-level patient safety priorities.
- Supervised personnel may be effectively deterred from providing routine, low-level alleviative care.
- Medically insignificant, low-quality data collections would be incompatible with PRA principles—the added burdens and wasteful allocations of licensee/regulator resources would outweigh any benefits of NRC compiling such data.

Although the proprietary dose-estimation methodology of PRM-35-22 was effectively rejected by the Commissioners' directive to focus on radiation safety and outcomes (SRM-SECY-22-0043), any reporting approach in regulation or guidance based on third-party tools or novel methodologies would likely have the following negative consequences:

- Added costs and burdens for patients.
- Healthcare facility costs and burdens associated with hardware tools, software subscriptions, dedicated FTE personnel, or other materials needed for the process of reportability determinations.
- Patient scheduling issues and decreased access to imaging and therapeutic procedures based on availability and allocation of sterile devices and/or FTE personnel within each individual facility.
- Nationwide reliance by thousands of healthcare facilities and 20 million patients each year on a single vendor or small number of vendors for requisite compliance devices and accessories. This threatens supply chain unsustainability which could result in shortages with delayed cancer treatments, delayed patient disease/condition diagnoses, procedure cancelations, wasted radiopharmaceutical doses, etc.
- Any tool-based NRC compliance methods could potentially conflict with FDA/manufacturer-understood medical device labeling and intended use of such devices.
- Low-quality data collection would generally be incompatible with PRA principles and requirements.

The ACR welcomes further communications with NRC about this rulemaking. Please contact Gloria Romanelli, JD, Senior Director, Legislative and Regulatory Relations and Legal Counsel, Quality and Safety, at gromanelli@acr.org; or Michael Peters, Senior Government Affairs Director, at mpeters@acr.org, with questions.

Sincerely

Jacqueline A. Bello, MD, ~~FACR~~
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