U.S.NRC
United States Nuclear Regulatory Commission
Protecting People and the Environment

Public Meeting:
U.S. Nuclear Regulatory Commission Staff Evaluation of Extravasation

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Meeting Logistics

- Today's slides are available in ADAMS at ML20338A283
- Meeting audio is via WebEx – please ensure you are connected to the audio using your computer or phone.
- WebEx tips:
  - Close out background applications (even VPN)
  - Reduce other household streaming activities
- If computer audio is poor, try switching to phone audio.
- Participants are in listen-only mode until the discussion portion of the meeting, but feel free to submit a "Chat" comment at any time during the presentation.

Today's Meeting

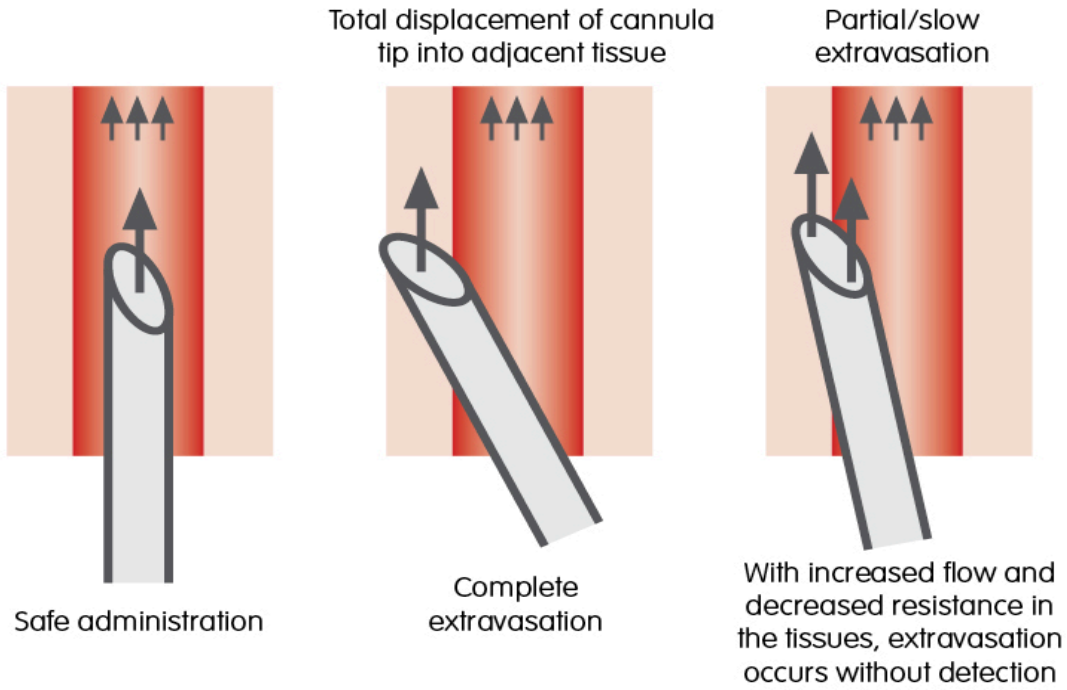
- The purpose of today's meeting is to get medical community and other stakeholder feedback on radiopharmaceutical extravasations, and whether they should be reported as medical events. This input will help inform the NRC staff's evaluation of the issue.
- Today's meeting is being transcribed.
- Today's meeting is separate from the recently closed public comment period on the petition for rulemaking (PRM-35-22).
  - To see those comments, go www.regulations.gov, search "PRM-35-22"

Meeting Agenda

- What is extravasation
- 1980 rule excluding extravasations from misadministration reporting
- The staff's evaluation of extravasations
- Congressional interest in reporting extravasations as medical events
- Discussion Questions and Public Comments
  - Injection quality monitoring
  - Classification
  - Reporting
  - Other factors and considerations

Extravasation

- Unintentional leakage of IV-infused "drug" into the tissue surrounding a vein or artery during administration.
- Medical issue not limited to radiopharmaceuticals.
- Studies indicate overall extravasation rate from 0.10 to 16% of injections.
- Patient anatomy; training, experience, and technique of medical personnel; inadequate catheter size.



Source: Managing chemotherapy extravasations in practice, Helen Roe MSc, www.hospitalpharmacyeurope.com

1980 Misadministration Reporting Requirements

- In a 1980 final rule (45 FR 31701) the Commission did not require licensees to report extravasations to the NRC.
- The Commission stated that “[e]xtravasation frequently occurs in otherwise normal intravenous or intraarterial injections. It is virtually impossible to avoid. Therefore, the Commission does not consider extravasation to be a misadministration.”

Why Re-Evaluate the 1980 Position?

- New radiopharmaceuticals since the 1980 final rule regarding Misadministration Reporting Requirements.
- Petition for rulemaking (PRM-35-22) requiring reporting of extravasation that exceed 0.5 Sv (50 rem) dose equivalent.
- Congressional interest urging action on extravasation.

Extravasation: NRC Staff Evaluation

- NRC staff will determine whether extravasations should be reported as medical events, and if so, what is the appropriate reporting threshold for these events?
- The staff's evaluation will be based on:
  - Is extravasation preventable with technology?
  - Is extravasation a practice of medicine concern or regulatory concern?
  - Is the dose consequence significant enough to merit a change and require regulatory reporting?

Next Steps

- NRC staff will provide the Advisory Committee on Medical Uses of Isotopes (ACMUI) the draft evaluation and options in January 2021.
- Staff will complete its technical evaluation in April 2021.
- Decision to accept or deny the petition is due in June 2021.

Congressional Interest in Extravasation

- House and Senate FY20 appropriation bills required a report on "updates to injection quality monitoring, classification, and reporting requirements regarding extravasations."
  - Congressional report submitted on March 17, 2020 (ADAMS Accession No. ML20050W302)
- House FY21 appropriation draft bill includes text on "Re-evaluation of Nuclear Medicine Event Reporting," requests a briefing on the topic.

Discussion Questions and Comments

- In addition to listening to your general comments, we have structured discussion questions around the following topics:
  - Injection quality monitoring
  - Classification of medical events
  - Reporting of medical events
  - Other factors and considerations

Injection Quality Monitoring

- The Medical Use Policy Statement (65 FR 47654) guides the NRC's regulation of the medical use of radionuclides as necessary to provide for the radiation safety of workers and the general public.
- The NRC encourages licensees to use quality assurance tools and available technology to ensure that the licensee delivers the administration that the physician intended.
- The NRC requires certain quality assurance procedures—such as calibrating instruments used to measure patient dosages and recording dosages administered—but there are many procedures that the NRC does not require.

Injection Quality Monitoring: Questions for Comment

- Do you monitor for radiopharmaceutical extravasation? If so, how?
- Do you expect that monitoring for extravasation and reviewing the results would improve radiopharmaceutical administration techniques?
- Is there technology than can prevent extravasation?
- Do you believe a regulatory action requiring monitoring and review of extravasation is appropriate?

Classification

- Currently, the NRC excludes extravasation of radiopharmaceuticals from its medical event reporting regulations.
- Medical events may not necessarily result in harm to the patient, but they can indicate a potential problem in a medical facility's use of radioactive materials and administration as directed by the physician.

Classification: Questions for Comment

- If we were to require reporting of extravasations that meet a medical event reporting criteria, should a distinction be made between reporting extravasations of diagnostic and therapeutic radiopharmaceuticals?
- Should a different dose threshold be developed for extravasation? Or should there be certain caveats (like with Y-90 microspheres)?
- If extravasations were classified as medical events, how would you make a dose estimation for an extravasation event?

Reporting

- The NRC tracks and trends medical events. The NRC may issue generic communications to share information about events with licensees. Recent examples include:
  - IN-2019-06, Patient Skin Contamination Events with I-131 MIBG
  - IN-2019-07, Methods to Prevent Medical Events
  - IN-2019-11, Sr-82/Rb-82 Generator Elution Events
  - IN-2019-12, Y-90 Medical Events
- Because licensees are not required to report extravasations to the NRC, extravasation events are not recorded in the NRC's Nuclear Material Events Database (NMED).

Reporting

- The NRC is aware of therapeutic extravasation resulting in medical follow-up:
  - Extravasation of lutetium-177 (Lu-177) resulted in an estimated dose of 8 +/- 4 Gy.
  - Extravasation of iodine-131 (I-131) MIBG in an estimated dose of 12-16 Gy.
  - Extravasation of yttrium-90 (Y-90) resulted in an estimated dose of 50 Gy to the treatment site. The site developed erythema after two days, dermatitis in the following weeks, and extensive cutaneous necrosis five months after injection.

Source: C J Martin, *et al.,* "Guidance on prevention of unintended and accidental radiation exposures in nuclear medicine" 2019 *J. Radiol. Prot.* **39** 665.

Reporting

- The events on the previous slide would not require reporting under the current paradigm.
- The events on the previous slide demonstrate that there are risks of tissue reactions in patients from extravasation during therapeutic injections involving β-emitters.
- The reported doses on the previous slide would trigger medical event reporting criteria for other medical use situations. Why report one and not the other?

Reporting: Questions for Comment

- What would be the burden, or unintended consequences, of medical event reporting of extravasations—on medical use licensees and the nationwide use of radiopharmaceuticals?
- What would be the benefit of reporting extravasations?
- If we were to require that licensees report extravasations as medical events, what reporting criteria should be used to enable the regulator to identify problems, monitor trends, and ensure that the licensee takes corrective action(s)?
- One of the reporting requirements is to determine why the event occurred; how would licensees make this determination?

Other Factors

- Patient (age, anatomy, physical condition, prior treatments)
- Radiopharmaceutical (dose and volume, radionuclide energy and emissions, injection rate, formulation)
- Dose Delivery (type of vascular access device, location of chosen vessel, hand injection versus power injection)
- Skill of person placing the vascular access

Other Considerations

- Terms: “Diffuses Out” versus “Extravasate”
- Are there any injection quality initiatives underway?
- How often are scans repeated due to radiopharmaceutical infiltration or extravasation?
- What else?