



**AMERICAN SOCIETY
FOR RADIATION ONCOLOGY**
251 18th St. South, 8th Floor
Arlington, VA 22202

Main: 703.502.1550
Fax: 703.502.7852
www.astro.org · www.ranswers.org

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May 19, 2022

Chairman Christopher Hanson
US Nuclear Regulatory Commission
Mail Stop O-16 B33
Washington, DC 20555-0001

Chairman Hanson:

On behalf of the American Society for Radiation Oncology¹ (ASTRO), I am writing to encourage you to follow the recommendations of the NRC's Advisory Committee on the Medical Use of Isotopes (ACMUI) regarding reporting extravasations as medical events.

On May 18, 2020, Lucerno Dynamics, LLC submitted a petition for rulemaking requesting the NRC revise its medical event reporting regulations to "require the reporting of extravasations that exceed a 0.5 Sv (50 rem) dose equivalent to tissue."

In its 1980 Misadministration Reporting Requirements Final Rule (Federal Register, Vol. 45, No.95, Page 31701-31704), the NRC defines extravasations as "the infiltration of injected fluid into the tissue surrounding a vein or artery." The NRC further states that "Extravasation 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." Extravasations are not unique to the administration of diagnostic or therapeutic radiopharmaceuticals and occur in other areas of medical care. Monitoring extravasations is a medical issue that is overseen by the licensee's quality management program.

Further, in 2019, an NRC Advisory Committee on the Medical Use of Isotopes (ACMUI) subcommittee reviewed the 1980 decision discussed above and concluded that "extravasation is a practice of medicine issue and not an item that needs to be regulated by the NRC." The subcommittee recommended that "extravasations that lead to 'unintended permanent functional damage' be reportable as a Medical Event under 10 CFR 35.3045(b)." ASTRO supports the ACMUI's recommendation and questions the need for rulemaking.

Additionally, we believe it is important to note that Lucerno Dynamics manufactures the Lara® System, which provides "quality control and quality assurance for nuclear medicine injections" by monitoring and detecting extravasations. Even without purchasing a Lara System, licensees would be forced to use additional time and resources, that are not otherwise reimbursed, to monitor for extravasation to comply with this suggested regulatory change for every radiopharmaceutical administration. More importantly, patients would be unnecessarily inconvenienced due to this additional required monitoring without a discernible benefit to patient safety. If the NRC proceeds with rulemaking, it will essentially be handing

an unfunded mandate to all licensees who administer radiopharmaceuticals, whether for diagnostic or therapeutic purposes. Additionally, ASTRO is concerned that the submission of the petition by a manufacturer of a device that would directly benefit from the change in regulations constitutes a conflict of interest and cautions the NRC in their decision making on this petition.

ASTRO opposes any option that would require additional dosimetry, a dose threshold, or the purchase of proprietary equipment to measure dose to determine whether an extravasation must be reported as a medical event. We believe that adding NRC oversight of extravasation will unnecessarily increase regulatory burden for licensees without a radiological or patient safety benefit.

In 2021, the NRC staff sent the Advisory Committee on the Medical Use of Isotopes (ACMUI) its evaluation on medical event reporting for extravasation. The evaluation included the following six potential options for radiopharmaceutical extravasation and medical event reporting:

1. **“No Action”** would maintain the status quo, and extravasations would continue to be excluded from medical event reporting.
2. **“50-rem dose threshold”** would require medical event reporting for extravasations that exceed a localized dose equivalent of 50 rem.
3. **“Administration site dose for procedures requiring a written directive”** would require that for procedures requiring a written directive, extravasations resulting in a dose 50 rem greater and 50 percent or more than the expected dose to the administration site be reported as medical events.
4. **“Extravasation events that require medical attention”** would be a non-dose based option for reporting extravasations that result in a radiation injury.
5. **“Extravasation events that cause a significant dose”** would require medical event reporting for extravasations that meet the 10 Gy (1,000 rad) dose threshold requirement for Abnormal Occurrences (AO).
6. **“Extravasation events that cause permanent functional damage”** would require extravasations that result in permanent functional damage to be reported as medical events.

In a report dated September 16, 2021, the ACMUI supported Option 4 (“Extravasation events that require medical attention”), stating that this option would “provide NRC with information on the types of radiation injuries caused by extravasation, and the frequency of such injuries.” As we mentioned earlier, monitoring extravasations is a medical issue that is overseen by the licensee’s quality management program. While ASTRO prefers Option 1 (“No action”), should the Commission determine that rulemaking is necessary, we strongly urge the NRC to follow the advice of its ACMUI and proceed with Option 4 (“Extravasation events that require medical attention”).

We appreciate the opportunity to work with the NRC on this important issue. Should you have any questions, please contact Cindy Tomlinson, Senior Patient Safety and Regulatory Affairs Manager at cindy.tomlinson@astro.org or 703.839.7366

Sincerely,



Laura I. Thevenot
Chief Executive Officer

CC:

Commissioner Jeff Baran
Commissioner David Wright

Attachments:

ASTRO Comments on Petition for Rulemaking: Reporting Nuclear Medicine Injection Extravasations as Medical Events [Docket No. PRM-35-22; NRC-2020-0141], November 30, 2020

ASTRO Letter to Dr. Darlene Metter, Chair, ACMUI, August 31, 2021

November 30, 2020

Kristine L. Svinicki, Chairman
Nuclear Regulatory Commission
Mail Stop O-4F00
Washington, DC 20555-0001

Re: Petition for Rulemaking: Reporting Nuclear Medicine Injection Extravasations as Medical Events [Docket No. PRM-35-22; NRC-2020-0141]

Dear Chairman Svinicki,

The American Society for Radiation Oncology (ASTRO) appreciates the opportunity to submit comments on the Reporting Nuclear Medicine Injection Extravasations as Medical Events petition for rulemaking, published in the Federal Register on September 15, 2020. ASTRO believes that adding NRC oversight of extravasation will unnecessarily increase regulatory burden for licensees without a radiological or patient safety benefit, and therefore we oppose rulemaking in this matter.

ASTRO is the largest radiation oncology society in the world, with more than 10,000 members who specialize in treating patients with radiation therapies. As the leading organization in radiation oncology, biology and physics, the Society is dedicated to improving patient care through education, clinical practice, advancement of science and advocacy. ASTRO's highest priority has always been ensuring patients receive the safest, most effective treatments.

The petition for rulemaking, filed by Lucerno Dynamics, LLC on May 18, 2020, requests the NRC to revise its medical event reporting regulations to "require the reporting of extravasations that exceed a 0.5 Sv (50 rem) dose equivalent to tissue."

In its 1980 Misadministration Reporting Requirements Final Rule (Federal Register, Vol. 45, No. 95, Page 31701-31704), the NRC defines extravasations as "the infiltration of injected fluid into the tissue surrounding a vein or artery." The NRC further states that "Extravasation 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." Extravasations are not unique to the administration of diagnostic or therapeutic radiopharmaceuticals and occur in other areas of medical care. Monitoring extravasations is a medical issue that is overseen by the licensee's quality management program.

Current medical event reporting requirements are found under [10 CFR 35.3045](#), *Report and notification of a medical event*. ASTRO believes that the requested change is unwarranted as extravasations, should they "exceed a 0.5 Sv (50 rem) dose equivalent to tissue", are reportable under either 10 CFR 35.3045(a)(1)(i) or 10 CFR 35.3045(b).

10 CFR 35.3045(a)(1)(i): A licensee shall report ... A dose that differs from the prescribed dose or dose that would have resulted from the prescribed dosage by more than 0.05 Sv (5 rem) effective dose equivalent, **0.5 Sv (50 rem) to an organ or tissue**, or **0.5 Sv (50 rem) shallow dose equivalent to the skin**; [Emphasis added.]

10 CFR 35.3045(b): A licensee shall report any event resulting from intervention of a patient or human research subject in which the administration of byproduct material or radiation from byproduct material **results or will result in unintended permanent functional damage** to an organ or a physiological system, as determined by a physician. [Emphasis added.]

In 2019, an NRC Advisory Committee on the Medical Use of Isotopes (ACMUI) subcommittee reviewed the 1980 decision discussed above, and concluded that “extravasation is a practice of medicine issue and not an item that needs to be regulated by the NRC.” The subcommittee recommended that “extravasations that lead to ‘unintended permanent functional damage’ be reportable as a Medical Event under 10 CFR 35.3045(b).” ASTRO supports the ACMUI’s recommendation and questions the need for rulemaking.

In a presentation to the ACMUI on March 30, 2020, NRC staff discussed 5 medical events using radiopharmaceuticals reported in 2019, including 2 events using Ra-223 dichloride, and 3 events using Lutetium-177. The descriptions presented to the ACMUI of the 5 events do not indicate extravasation occurred. Five reported events are a very small percentage when compared to CMS utilization data showing that there were approximately 3,000 therapeutic radiopharmaceutical infusions performed in 2018.

Additionally, as indicated in the self-reported data, none of the 28 out of 15,509 total events entered into RO-ILS: Radiation Oncology Incident Learning System¹ that were related to radiopharmaceuticals have been reported to either the NRC or an Agreement State.

Finally, we believe it is important to note that Lucerno Dynamics manufactures the Lara[®] System, which provides “quality control and quality assurance for nuclear medicine injections” by monitoring and detecting extravasations. Even without purchasing a Lara System, licensees would be forced to use additional time and resources, that are not otherwise reimbursed, to monitor for extravasation to comply with this suggested regulatory change for every radiopharmaceutical administration. More importantly, patients would be unnecessarily inconvenienced due to this additional required monitoring without a discernible benefit to patient safety. If the NRC proceeds with rulemaking, it will essentially be handing an unfunded mandate to all licensees who administer radiopharmaceuticals, whether for diagnostic or therapeutic purposes. Additionally, ASTRO is concerned that the submission of the petition by a manufacturer of a device that would directly benefit from the change in regulations constitutes a conflict of interest, and cautions the NRC in their decision making on this petition.

¹ RO-ILS is the only medical specialty society-sponsored radiation oncology incident learning system. Sponsored by ASTRO and the American Association of Physicists in Medicine (AAPM), the mission of RO-ILS is to facilitate safer and higher quality care in radiation oncology by providing a mechanism for shared learning in a secure and non-punitive environment.

Given the fact that extravasations, should they occur to the extent the petitioner recommends, are covered under the current regulations and the associated additional burden posed to licensees, we oppose any changes to the current regulations. We appreciate the opportunity to provide comments on this important issue. Should you have any questions, please contact Cindy Tomlinson, Senior Patient Safety and Regulatory Affairs Manager at cindy.tomlinson@astro.org or 703.839.7366.

Sincerely,

A handwritten signature in black ink that reads "Laura Thevenot". The signature is written in a cursive, flowing style.

Laura I. Thevenot
Chief Executive Officer

August 31, 2021

Dr. Darlene Metter
Chair, Advisory Committee on the Medical Use of Isotopes
US Nuclear Regulatory Commission
Washington, DC 20555-0001

Dear Dr. Metter,

The American Society for Radiation Oncology¹ (ASTRO) commends the Nuclear Regulatory Commission's (NRC) Advisory Committee on the Medical Use of Isotopes' (ACMUI) Subcommittee on Extravasation on their thorough review of the NRC staff's preliminary evaluation of radiopharmaceutical extravasation and medical event reporting.

In its evaluation, the NRC staff outlined six potential options for radiopharmaceutical extravasation and medical event reporting:

1. **“No Action”** would maintain the status quo, and extravasations would continue to be excluded from medical event reporting.
2. **“50-rem dose threshold”** would require medical event reporting for extravasations that exceed a localized dose equivalent of 50 rem.
3. **“Administration site dose for procedures requiring a written directive”** would require that for procedures requiring a written directive, extravasations resulting in a dose 50 rem greater and 50 percent or more than the expected dose to the administration site be reported as medical events.
4. **“Extravasation events that require medical attention”** would be a non-dose based option for reporting extravasations that result in a radiation injury.
5. **“Extravasation events that cause a significant dose”** would require medical event reporting for extravasations that meet the 10 Gy (1,000 rad) dose threshold requirement for Abnormal Occurrences (AO).
6. **“Extravasation events that cause permanent functional damage”** would require extravasations that result in permanent functional damage to be reported as medical events.

The ACMUI subcommittee reviewed the staff's options and is supporting Option 4 (“Extravasation events that require medical attention”). In its report, the subcommittee stated that Option 4 would “provide NRC with information on the types of radiation injuries caused by

¹ ASTRO is the largest radiation oncology society in the world, with more than 10,000 members who specialize in treating patients with radiation therapies. As the leading organization in radiation oncology, biology and physics, the Society is dedicated to improving patient care through education, clinical practice, advancement of science and advocacy. ASTRO's highest priority has always been ensuring patients receive the safest, most effective treatments.

extravasation, and the frequency of such injuries.” ASTRO believes that adding NRC oversight of extravasation will unnecessarily increase regulatory burden for licensees without a radiological or patient safety benefit, and therefore prefers Option 1 (“No action”). Monitoring extravasations is a medical issue that is overseen by the licensee’s quality management program.

ASTRO opposes any option that would require additional dosimetry, a dose threshold, or the purchase of proprietary equipment to measure dose to determine whether an extravasation must be reported as a medical event. Therefore, we oppose Option 2 (“50-rem dose threshold”), Option 3 (“Administration site dose for procedures requiring a written directive”), and Option 5 (“Extravasation events that cause a significant dose”).

If, however, the NRC is determined to require reporting on extravasations, and given the options presented, ASTRO is generally supportive of Option 4 (“Extravasation events that require medical attention”) or Option 6 (“Extravasation events that cause permanent functional damage”).

We do have concerns that under Option 4, the term “medical attention” is ambiguous and raises more questions than it answers. For example, what is the definition of “medical attention”? What intensity of medical attention triggers the reporting mandate? Under this option, a patient noticing a red mark or swelling and merely going to talk to their physician—regardless of whether radiation was the cause—would trigger a medical event report. Or is it something more complicated and serious, like a non-healing skin ulcer or skin and soft tissue necrosis that requires medical intervention?

A patient may not seek medical attention until well after the administration of a radiopharmaceutical, and in the rare case that an expert determines the cause of the red mark or swelling is from radiation and requires medical intervention—such as applying hyperthermia—then a medical event report is reasonable. Therefore, ASTRO recommends the ACMUI change “Extravasation events that require medical attention” to “Extravasation events that require medical *intervention for a suspected radiation injury*”.

We appreciate the opportunity to provide comments on this important issue. Should you have any questions, please contact Cindy Tomlinson, Senior Patient Safety and Regulatory Affairs Manager at cindy.tomlinson@astro.org or 703.839.7366.

Sincerely,



Laura I. Thevenot
Chief Executive Officer

Chairman Resource

From: Cindy Tomlinson <cindy.tomlinson@astro.org>
Sent: Thursday, May 19, 2022 3:14 PM
To: Chairman Resource
Subject: [External_Sender] ASTRO Letter re: Extravasation
Attachments: FINAL ASTRO Extravasation Letter to Commissioners May 19 2022.pdf

Good afternoon.

Please find attached a letter from the American Society for Radiation Oncology (ASTRO) on reporting extravasation as a medical event.

Should you have any questions, please feel free to contact me.

Best,

Cindy Tomlinson, MPP
Senior Patient Safety and Regulatory Affairs Manager
American Society for Radiation Oncology (ASTRO)
251 18th St. South, 8th Floor
Arlington, VA 22202
703-502-1550 main
703-839-7366 direct
703-839-7367 fax
www.astro.org
www.rtanswers.org