U.S. Nuclear Regulatory Commission
Advisory Committee on the Medical Use of Isotopes
Subcommittee on Extravasation

***Draft Report* Submitted on: August 15, 2019**

Subcommittee Members: Vasken Dilsizian, M.D., Richard Green, Melissa Martin (Chair), Michael Sheetz, Megan Shober, Laura Weil
NRC Staff Resource: Said Daibes, PhD (formerly Maryann Ayoade)

Subcommittee Charge:

Re-evaluate and provide recommendations on the NRC decision on infiltrations and extravasations published in the Federal Register, Volume 45, No. 95, on May 14, 1980.

Background:

The subcommittee and its Chair were appointed by ACMUI Chairman, Dr. Christopher Palestro, at the ACMUI meeting on April 3, 2019. The purpose of the subcommittee was to review the NRC current decision on infiltrations and extravasations when radionuclides are injected into patients which was published in the Federal Register, Volume 45, No. 95, Page 31701-31704 on May 14, 1980. The following specific requirements are pertinent to this request for review.

"Extravasation is the infiltration of injected fluid into the tissue surrounding a vein or artery. Extravasation frequently occurs in otherwise normal intravenous or intra-arterial injections. It is virtually impossible to avoid. Therefore, the Commission does not consider extravasation to be a misadministration."

The criteria for a misadministration as outlined in this publication is:
§ 35.41 Definition of a misadministration.
For this part, misadministration means the administration **of:**
(a) A radiopharmaceutical or radiation from a sealed source other than the one intended;
(b) A radiopharmaceutical or radiation, to the wrong patient;
(c) A radiopharmaceutical or radiation by a route of administration other than that intended by the prescribing physician;
(d) A diagnostic dose of a radiopharmaceutical differing from the prescribed dose by more than 50 percent;
(e) A therapeutic dose of a radiopharmaceutical differing from the prescribed dose by-more than 10 percent; or
(f) A therapeutic radiation dose from a sealed source such that errors in the source calibration, time of exposure and treatment geometry result in calculated total treatment dose differing from the final prescribed total treatment dose by more than 10 percent.
(Ref: Section 35.41as published in the Federal Register, Volume 45, No. 95 on May 14, 1980)

In 2002, current medical event definition was changed from misadministration as published in the Federal Register at the following reference: 10 CFR 35.3045 "Report and Notification of a Medical Event."

At the April 3, 2019 meeting of the ACMUI, a presentation was made regarding a technology, which may help identify extravasations. The goal for the use of this product is to reduce the frequency extravasations. Data was presented relative to this product's use for PET isotope injections and the effect on Standardized Uptake Value (SUV) of tumors or organs when extravasation occurs. There was a request for the NRC to review 1980 policy exemption due to extravasation.

Discussion:

The subcommittee again discussed the topic of extravasation of radiopharmaceuticals at the injection site. This topic has been discussed at two previous ACMUI meetings (December 18, 2008 and May 8, 2009) with the decisions made that this not be reported as a medical event at the current time.

- **Clinical aspects of the occurrence of extravasation of radiopharmaceuticals**: The main point of this discussion is that the denominator for this problem is several million injections per year of all radiopharmaceuticals used. The problem is not limited to PET isotopes only. If an extravasation occurs to the extent that the image quality is compromised, the procedure is repeated the following day or shortly thereafter at the discretion of the authorized physician. The prevention of extravasation is a medical training issue for the authorized user (AU) physician and the technologist under the supervision of the AU, which is considered medical practice and not something that needs NRC regulation.

- There are currently 48 radiopharmaceuticals approved by the FDA (including five IV therapeutic drugs). Extravasation of the six fluorinated compounds including the F-18 PET drugs can bring about discrepancies in the SUV. However, the SUV value is not relied on solely. It is one way to give a quantified value to the images. It is common to have some remaining isotope at the injection site. For isotopes other than FDG isotopes used for PET, it is difficult to quantify non F-18 drugs left at the injection site and difficult to assign the radiation dose attributable to it. When extravasation of radiopharmaceuticals occurs, there will be a variable delay in the biodistribution after injection. None of the total doses in these extravasations meet the NRC's medical event criteria of a discrepancy of a total dosage of +/- 20% delivered dose criteria. This subcommittee does not consider extravasation a defacto medical event.

- Extravasation frequently occurs in otherwise normal intravenous or intraarterial injections and is virtually impossible to avoid. While there are devices in the market today that can identify extravasation, not all cameras (PET and SPECT) can quantify for all radiopharmaceuticals. These methods do not quantify the amount of activity that is infiltrated but it does alert personnel to the occurrence of an infiltrate. Members of this subcommittee are unaware of any cases where there has been patient harm due to extravasation as of today.

Subcommittee Recommendations:

- Extravasation is a practice of medicine issue and not an item that needs to be regulated by the NRC.

- The subcommittee recommends that extravasations be considered a type of passive "patient intervention", similar to the recommendations from the ACMUI subcommittee (presented during the ACMUI public meeting on October 2015 and referenced in the Patient Intervention subcommittee report dated April 27, 2017), and should be captured in the NRC's current definition of patient intervention under 10 CFR 35.2.

- There is no evidence at this time for this subcommittee to recommend a reclassification of extravasation at the injection site for radiopharmaceuticals to be considered a medical event. The subcommittee recommends that extravasations that lead to "unintended permanent function damage" be reportable as a Medical Event under 10 CFR 35.3045(b).

One member of the subcommittee had a different perspective on potential medical event reporting due to extravasation. Her minority opinion is included here, in its entirety.

One member of the Subcommittee expressed concern with the existing 1980 exclusion of extravasation events from ME status. This member acknowledges the Subcommittee consensus that there would be only rare incidence of extravasation triggering ME criteria of >50 rem tissue dose or <80% of prescribed dose delivered to the patient, and believes the extravasation exemption in the 1980 language is unnecessary. Only rare gross discrepancies in delivered dose or tissue exposure would be reportable, and this member believes that those rare instances should be reported just as any other misadministration of such magnitude would be reported as MEs. The fact that they may result in no patient harm should have no bearing on the requirement to report. This would be consistent with the fact that all other ME's that cause no patient harm are currently required to be reported. When/if NRC decides to redefine ME criteria to exclude events that do not cause patient harm, then extravasation incidents would be included in such exclusion. But this member believes that the current specific exclusion of extravasation is inconsistent with other regulation and unwarranted.
Respectfully submitted,
Laura Weil

Respectfully submitted on August 15, 2019,
Subcommittee on Extravasation
Submitted to:
Advisory Committee on the Medical Use of Isotopes (ACMUI),
Nuclear Regulatory Commission (NRC)