Statement of
The American Society for Radiation Oncology (ASTRO)
Before the Nuclear Regulatory Commission's Advisory Committee on the Medical Use of Isotopes
March 10, 2016

Chairman Alderson, members of the ACMUI and NRC staff, thank you for allowing me to provide this statement on training and experience (T&E) requirements for the administration of radiopharmaceuticals on behalf of the American Society for Radiation Oncology (ASTRO).

My name is Gregg Franklin and I am a radiation oncologist with the New Mexico Cancer Center. As part of my practice, I administer radiopharmaceuticals such as I-131 for thyroid cancer, Ra-223 (Xofigo) for prostate cancer, Y-90 (Zevalin) for lymphoma as well as many others. As an authorized radiation oncologist in NM giving radiopharmaceuticals, I have a lot of experience with their delivery and side effects, as well as the challenges inherent in their utilization.

I am also a member of ASTRO - 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.

Radiopharmaceuticals
Radiopharmaceuticals, including Zevalin, are highly effective in treating cancer, but also potentially hazardous drugs with possible harmful effects to both the patient and the public if not used correctly and under the supervision of a highly trained physician. ASTRO strongly opposes any reduction in the training and education (T&E) requirements found in 10 CFR 35.390, *Training for use of unsealed byproduct material for which a written directive is required*. Under this section, the NRC requires an authorized user (AU) to be certified by a medical specialty board recognized by either the NRC or an agreement state, or has completed 700 hours of T&E in "basic radionuclide handling techniques applicable to the medical use of unsealed byproduct material requiring a written directive." ASTRO believes that these requirements are appropriate, protect the safety of patients, the public, and practitioners, and should not be changed.

On March 20, 2006, William Stein, III, MD filed a petition for rulemaking requesting "the codification of the 80-hour training and experience requirement as appropriate and sufficient for physicians desiring to attain AU status limited to therapeutic administrations of ^{153}Sm-lexidronam (Quadramet), ^{131}I-tositumomab (Bexxar) and ^{90}Y-ibritumomab tiuxetan (Zevalin), all FDA-approved parenterally-administered therapeutic agents." ASTRO submitted comments opposing the petition for rulemaking on August 28, 2006 stating that "Decreasing the training required for physicians to administer radiopharmaceuticals places the patient at risk for higher rates of misadministration and treatment-related toxicities. Significant knowledge regarding radiation dose distribution, radiation dose tolerance of normal tissues, and the safe use and handling of radiopharmaceuticals cannot be imparted with limited training." The NRC subsequently denied this petition for rulemaking on October 27, 2007, stating that "the current NRC regulations at 10 CFR 35.390 and 35.396 establish the appropriate amount of training and experience for a physician to become an authorized user for the parenteral administration of unsealed byproduct material requiring a written directive, including Quadramet, Bexxar and Zevalin." Bexxar was ultimately pulled from the market in 2014 because of lack of use. Quadramet and Zevalin are still in use.

Recently, we have become aware of a renewed push to reduce the T&E requirements for radiopharmaceuticals based on concerns about a shortage of AUs for the administration of Zevalin. ASTRO continues to object to a reduction in the T&E requirements based on a threat to the safety of patients and the public and a lack of data to support a shortage of AUs. The NRC's focus on patient safety and the safety of the general public as it develops T&E requirements is appropriate. With this in mind, the NRC determined that the level of training required to administer these treatments must include either board certification or 700 hours of training and experience. The NRC intentionally designed these requirements to allow new agents to come to market, so the NRC does not have the burden of writing different regulations for every new drug that is developed. The rule was intended to classify agents by their similar properties and particular risk profiles. The classroom and clinical experiences encompassed by radiation oncology and nuclear medicine training programs provide appropriate levels of knowledge and skill for any current and future radioactive agents. ASTRO supports the NRC's intent to craft a generally applicable rule rather than one that necessitates a specific review of each new radionuclide that becomes commercially available.

The rigorous T&E requirements contribute to the excellent safety record of radiopharmaceuticals. We believe that it is important that the person administering the radiopharmaceutical is appropriately trained in the safe handling, exposure risks, and the management of side effects of radiation. We do not believe that an 80 hour course will adequately cover these topics.

Administering radiopharmaceuticals is not as simple as ordering a patient-ready dose from a radiopharmacy and injecting it into a patient. In general, clinics administering radiopharmaceuticals follow these steps:

1. The AU develops the general policies, the standard operating procedures, and the quality assurance checks for their radiopharmaceutical program.
2. The AU ensures that good radiation protection procedures are followed throughout the procedure.
3. The AU determines whether or not it is appropriate for the patient to receive the radiopharmaceutical.
4. The patient receives any required pre-treatment laboratory and/or imaging studies.
5. The AU must determine the required dose and will enter the dose into the written directive.
6. The AU orders any additional medications and or drugs prior to delivery of the radiopharmaceutical.
7. The radiopharmaceutical is received from the radiopharmacy in either the nuclear medicine, radiology, or radiation oncology department. (This is determined by the facility, and may vary from site to site.)
8. The receiving department checks that the dose from the radiopharmacy is correct and accurate.
9. The AU confirms that the dose is correct and accurate. If there is an error to the dose, the AU will need to make a decision on how to proceed.
10. The AU administers the radiopharmaceutical, or will supervise the administration by appropriately trained personnel.
11. The AU monitors adverse reactions of the patient and handles any radioactive spills that may have occurred.

The above description assumes that the ordering, receiving, administration, and clean up goes as planned. However, without proper and extensive training, how will the AU know how to clean spills? How will the AU understand limits of dose variation? Will the AU know how to use a dose calibrator to assess the dose, and change it if necessary? Will the AU know how to dispose of tubing and syringes? What about flushing the IV? Will the AU know how to use a Geiger counter to detect a spill? Will the AU know how to handle a person who is accidentally contaminated? Will the AU be able to appropriately and competently supervise ancillary staff? Will an AU know how to handle the accidental delivery into the interstitial tissues of the body (i.e. "IV infiltration") or into an artery? Will the AU be able to make appropriate decisions based on radiobiology and the effects of multiple prior therapies on the patient (ie., external beam therapy)?

Ultimately, it is the AU who is responsible for the safety of the patient, the providers, and the public. It would be irresponsible to leave this to someone with inadequate training and experience.

In addition to ensuring patient safety, ASTRO is unaware of data that suggests a shortage of AUs. ASTRO asked NRC staff for the number of AUs licensed under 35.390 to assess whether there is a shortage of AUs, but learned that the NRC only tracks AUs licensed under 35.300. Without being able to identify which AUs are licensed under 35.390 and 35.300, it is not possible to confirm whether there is an actual AU shortage or a perceived one. Additionally, ASTRO has not heard what would be an ideal number of AUs. ASTRO estimates that there are approximately 2,200 radiation oncology facilities in the United States, which means aside from the many nuclear medicine trained AUs nationwide, there are likely enough AUs just among the radiation oncologists nationwide. Indeed, ASTRO is not aware of a perceived shortage of radiation oncologists anywhere in the country. ASTROs members are ready to care for patients needing any radiopharmaceutical.

We do not believe the available data on AUs supports a change in the T&E requirements. Instead, we believe other factors are influencing the use of Zevalin, most notably the availability of alternative treatments, including chemotherapy agents such as maintenance Rituximab. It is unlikely that a change in the T&E requirements will impact use of Zevalin, but could instead have the unintended consequence of exposing patients, providers, and the public to risks that could otherwise be avoided. Since there is no underlying public need for expansion of authorized users, the public should not be placed in a position of heightened and unnecessary risk, and therefore the T&E requirements should remain as written.

In addition, the NRC's Advisory Committee on the Medical Use of Isotopes (ACMUI) tasked a subcommittee to determine "if the current requirement of 700 hours for training and experience for authorized users … places hardship on the patient community." In its March 10, 2016 report, the subcommittee notes that even in "many large medical centers with an abundance of clinicians and AUs who work closely together, these radiopharmaceuticals are used infrequently." Further, the subcommittee was unable to conclude that the current T&E requirements have caused the decreased use of radiopharmaceuticals, including Zevalin, and "because of the potential issues raised by the proposed changes in T&E, the subcommittee recommends against the reduction in the number of hours of T&E required for 10 CFR 35.396 use." ASTRO agrees with this recommendation. ASTRO also agrees with the subcommittee's recommendation for the establishment of a standing committee to periodically review the current T&E requirements currently in effect and make recommendations for changes as warranted.

Part 35 Rulemaking

ASTRO is concerned that if the NRC decides to make changes to the T&E requirements, that doing so within the current Part 35 rulemaking will cause significant delays in the publication of the final rule. The Part 35 final rule will add a much needed and appropriate activity-based definition for medical events for permanent implant brachytherapy. ASTRO strongly opposes any further delays in the Part 35 rulemaking because without this definition there will continue to be much confusion surrounding medical events for permanent implant brachytherapy.

Conclusion

In conclusion, for the numerous reasons stated above, ASTRO opposes a reduction in the T&E requirements for 10 CFR 35.390, and supports the ACMUI subcommittee's recommendations to form a permanent committee to look at the requirements and make suggestions for changes as warranted.