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Training and Experience Requirements for Different Categories of Radiopharmaceuticals

Comment On: NRC-2018-0230-0001
Training and Experience Requirements for Different Categories of Radiopharmaceuticals

Document: NRC-2018-0230-DRAFT-0113
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General Comment

See attached file(s)

Attachments

UPPI AU Letter_100316

NRC Comments FINAL

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Docket: NRC-2018-0230 Training and Experience Requirements for Different Categories of Radiopharmaceuticals

Commenter: John Witkowski, President, UPPI

January 29, 2019

UPPI LLC (UPPI) appreciates the process that the NRC has instituted to consider whether to expand access to medical isotopes, and if so, how such increased access can be accomplished safely and effectively. UPPI strongly supports the Commission's willingness to proactively reach out to and consider diverse opinions on the training and education required for Authorized Users, and particularly appreciates the multiple opportunities that the Commission has provided for UPPI and our members to engage with the Commission and share our experience and ideas. We believe that the open and thoughtful process that the NRC has engaged in will enable it to expand access to vital medical tests and treatment while protecting safety.

UPPI has provided several comments to the Commission on why access should be expanded and how nuclear pharmacists can play a role in achieving that expansion.[1]

We reiterate those comments again here, but wanted to expand upon the several points that we believe will help clarify and enhance our proposal and several of the points we have made previously, and will add some more context and urgency to the need to increase access.

Specifically, in previous comments UPPI has suggested that the Commission consider enabling nuclear pharmacists, who have the same 700 hours of training as physician Authorized Users, (AUs), to provide the "Authorized User component" to a "Dual Authorized User" engagement with a limited training oncologist or other provider.

However, in conversations with NRC Commissioners and staff, we have realized that while the term "Authorized User" is understood in the nuclear pharmacist community to have one

[1] ADAMS: https://adamswebsearch2.nrc.gov/webSearch2/main.jsp?AccessionNumber=ML19019A023; https://adamswebsearch2.nrc.gov/webSearch2/main.jsp?AccessionNumber=ML19014A270; https://adamswebsearch2.nrc.gov/webSearch2/main.jsp?AccessionNumber=ML19002A614; https://adamswebsearch2.nrc.gov/webSearch2/main.jsp?AccessionNumber=ML19002A566. In addition, UPPI's original proposal was not uploaded to ADAMS, but is included as part of this submission.

meaning, it has a different meaning for the Nuclear Regulatory Commission. Specifically, for the NRC, the term "Authorized User" is defined by 35.2 as a "*Authorized user* means a physician, dentist, or podiatrist." However, there is a separate definition and requirements for an "Authorized nuclear pharmacist" under 10 CFR 32 and UPPI in its proposal unintentionally conflated those terms, which may have led to some confusion and misunderstanding on the part of the NRC as to what we are suggesting.

Specifically, UPPI is NOT suggesting that the definition of "Authorized User" be changed to include nuclear pharmacists, which we believe was the understanding of what our proposal was seeking. Instead, we are requesting that an "Authorized Nuclear Pharmacist" who has the same 700 hours of training as an Authorized User, be permitted to serve the nuclear safety role that the Authorized User would provide in administering alpha and beta emitters.

Therefore, in our previously proposed concept of having "dual Authorized Users" working as a team for the purpose of providing alpha and beta radiotherapy, we urge the Commission to read that proposal as requesting that a "Authorized Nuclear Pharmacist" be permitted to team with a limited-trained Authorized User (AU) medical oncologist or hematology oncologist, working on site with a Authorized *nuclear pharmacist* with the 700 hours training and experience criteria. Clearly, the limited-trained AU would be the person to treat the patient with the radiotherapy and would handle medical related responses. The Authorized Nuclear Pharmacist would be present and be directly responsible for the safe use of the radiopharmaceutical at the licensed site.

We reiterate that this approach would have a number of benefits. First, the Authorized Nuclear Pharmacist would be accessible to travel on site to locations, for example through a pre-arranged assignment. These radiotherapies are not emergency procedures and can be scheduled for a particular day to enable the team to get together. Second, the limited trained physician is a subset of the larger medical oncologist and hematology oncologist community. Therefore, licensing of sites for the administration of the radiotherapy would be a limited number. It is also not intended to suggest that a nuclear pharmacy would be the site of patient injection, as some public commenters have implied.

This proposal would enable the NRC to meet its safety and training requirements by ensuring that a trained and licensed individual is present at the time the nuclear pharmaceutical is administered to ensure the safety of the patient and the environment, and that proper protocols are met, while providing additional opportunities for expanding the administering of alpha and beta emitters.

It would also expand the availability of treatment options for patients, enabling patients to obtain treatment in more locations than are available currently. Further, it would enable

patients more access to the new and effective biological approaches utilizing alpha and beta radionuclides that continue to expand as new therapies for prostate, breast and other cancers will create a need for more AUs. UPPI believes that an expanded alternative pathway for T&E in the radiotherapy utilization of alpha and beta emitters is appropriate and necessary to allow patient access to these treatments.

As previously stated, there are training program alternatives that are currently available for the limited-trained physician.[2] We believe a structure can be established to set effective and appropriate training criteria and site licensing to allow a team approach in alpha and beta radiotherapies as we have proposed. Like some existing programs for AU qualification, we suggest the limited-trained physician observe three therapies, as an example, to understand handling and care of the patient who has undergone the therapy.

By way of background, the nuclear pharmacy ("NP") community plays an important role in ensuring patient safety. Centralized nuclear pharmacies handle the preparation and dose requirements for hospitals and diagnostic imaging centers by dispensing and delivering individually prescribed and calibrated patient specific dosages treatments for patients for molecular imaging. Across the country 300+ nuclear pharmacies cover metro, suburban and rural areas. NPs play a vital role in the distribution and administration of alpha and beta emitter therapies. UPPI members provide almost 25% of all doses delivered nation-wide every day.

Additional radiation safety training has recently been added to enable nuclear pharmacists to operate the RadioGenix™ Mo99/Tc99m generator system -a newly approved automated radionuclide elution system.[3]

We would also like to reiterate why this expansion in the availability of these treatments to patients is so important.

First, as discussed before, the number and type of alpha and beta emitter therapies that are in development is significant, and there likely to be broad demand for these therapies. This increase in demand will significantly tax the current system.

Second, without a significant expansion in treatment options, this increase in demand for nuclear therapies will further strain the already over-taxed rural healthcare system, making the availability of treatments for rural populations even more scarce than it already is. Specifically, as stated previously, certain patient populations, such as rural areas, are already disadvantaged

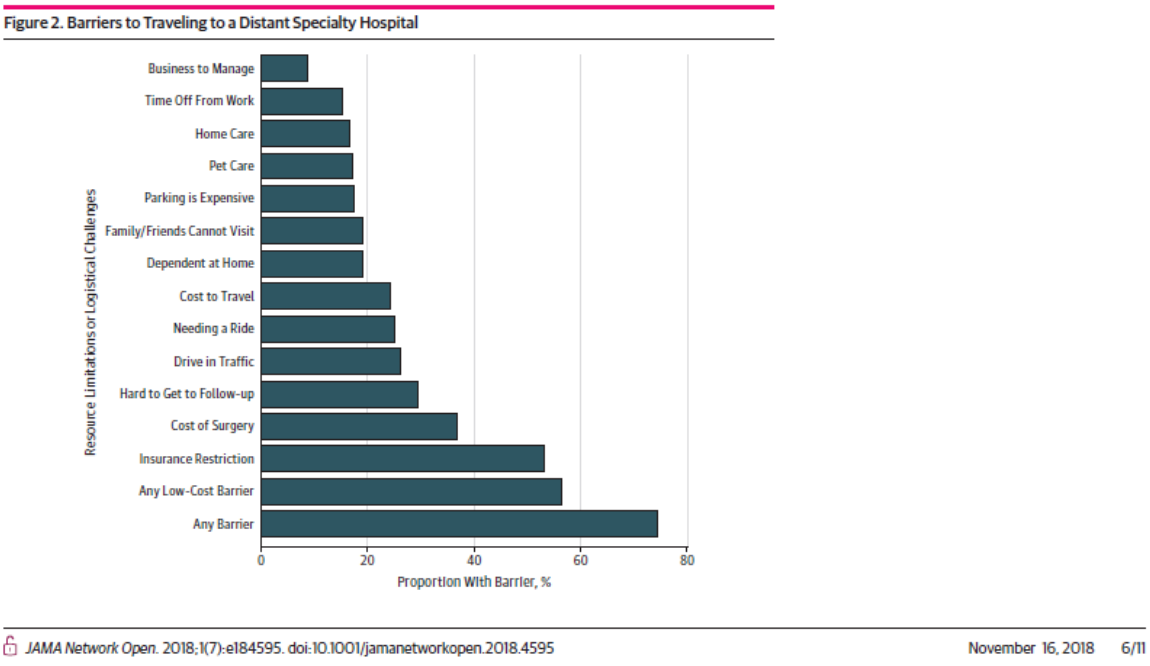
[2] ML16084A168

[3] https://www.nrc.gov/docs/ML1733/ML17338A449.pdf

in the distribution and availability of AUs because of hardships and distance, which could be barriers to treatment.

For example, in an article for the Journal of the American Medical Association Network, Benjamin J. Resio, et.al. looked at motivators, barriers and facilitators to traveling for complex cancer surgery to a *distant* specialty hospital, and found that at least 74% of all respondents experience at least one barrier that inhibits their ability to obtain treatment. [4] The challenges posed by these barriers to treatment would be magnified in the case of alpha and beta radiotherapy because these regimen are likely to require multiple treatments over a period of time.

It is noteworthy that this applies to *distant* hospitals – expanding the availability of treatment options and bringing them closer to the patient, as UPPI's proposal is designed to do, would alleviate many of these challenges.



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A solution is enabling a limited-trained Authorized User to team with an Authorized Nuclear pharmacist, with 700 hours of training, for the purposes of radiation safety and radiation protection. A limited trained physician teamed with a NP will satisfy the NRC concern for safety and care of the patient for the growing applications in alpha and beta radiotheranostics.

[4] https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2714502
[5] https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2714502

Thank you very much for your consideration of this alternative, and we look forward to answering any questions that you may have.

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October 3, 2016

Chairman Stephen G. Burns
U.S. Nuclear Regulatory Commission
Mail Stop O-16G4
Washington, DC 20555-0001

Re: Training and Experience Requirements for Alpha and Beta Emitters Patient Ready Doses

Dear Chairman Burns:

I'm writing to you with interest concerning the training and experience requirements of Authorized Users (AU) for alpha and beta emitters in patient ready doses. UPPI is an alliance of independent commercial radiopharmacies and leading non-profit academic medical center radiopharmacies, which are focused on delivering prepared radiopharmaceuticals for diagnostic molecular imaging and therapeutic patient care needs. UPPI national reach provides daily and on-call radiopharmaceuticals in metropolitan, secondary and tertiary, rural, market places. Every day UPPI member and affiliate pharmacies provide over 8,000 unit dose prescriptions for diagnostic imaging and radiotherapy to nuclear medicine physicians, radiologists, nuclear cardiologists and oncologists. The UPPI network includes 77 radiopharmacies and academic radiopharmacies and 10 cyclotrons for the production of Positron Emission Tomography (PET) radiopharmaceuticals.

We believe that the NRC should review the 700 hours of training and experience (T&E) requirements for AU, in 10 CFR 35.390 (training for the use of unsealed byproduct material for which a written directive is required) that might place a hardship on the patient community, and whether a change in the requirement for other medical specialists would be adequate and, more importantly, beneficial by expanding the geographic points of care for cancer patients.

Over the past months, I've followed the discussions regarding the release of the Advisory Committee on the Medical Uses of Isotopes (ACMUI) Final Report on Training & Experience for Authorized Users of Alpha and Beta Emitters under 10 CFR 35.390 submitted on

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March 16, 2016. That report recommended against the reduction of the number of T&E hours required for 10 CFR 35.390 use.

We believe there is another way to address the AU T&E situation without a reduction to the 700 hour requirement. The solution we proffer would allow a nuclear pharmacist, who already possesses the 700 hours T&E per 10 CFR 35.390, to work in direct concert with the physician specialist, oncologist or other specialist, in the administration of the patient prepared dose. The requests to change the required T&E previously submitted had centered toward opening the availability of the alpha and beta emitting therapeutic radiopharmaceuticals in order to reduce the hardship of patient access to these treatments. The question became that of maintaining the requirements for radiation safety, the proper handling of the radiopharmaceutical on site during administration of the drug to the patient (which had little discussion) and the immediate medical care needs of the patient at the time of the procedure that can be fulfilled by the physician specialist. The proposal we offer is teaming on-site of the nuclear pharmacist and the specialist physician whereas the nuclear pharmacist fulfills the AU requirement and works with the physician specialist, in direct supervision, during the injection of the radiopharmaceutical. The specialist physician handles the patient care aspects during and after the radiopharmaceutical administration. The nuclear pharmacist provides the survey and handling expertise before, during and after the administration of the radiotherapy.

There are approximately 350 radiopharmacies located throughout the United States and more than 1,000 practicing nuclear pharmacists. Nuclear pharmacists possess documented T&E that allows the individual to be listed on Radioactive Materials Licenses (NRC and Agreement State) as the AU and the Radiation Safety Officer. The Board of Pharmacy Specialties (BPS), in its fortieth year, established its first and longest running board certification in the practice of nuclear pharmacy. *"Nuclear Pharmacy seeks to improve and promote public health through the safe and effective use of radioactive drugs for diagnosis and therapy."* is found as the opening statement in the section on the Nuclear Pharmacy Specialty description on the BPS website.

Nuclear pharmacists dispense radiotherapeutic products on prescription as a normal course of clinical service. Radioiodine therapy has long been established in the diagnosis and treatment of thyroid disease, including thyroid carcinoma. The ACMUI final report of March 16,

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2016 recognized that endocrinologists, a specialist physician, have a "long history of familiarity with the use of radioactive materials." The radioiodine therapy, solution or capsule, is typically dispensed by the nuclear pharmacist (not the endocrinologist –who orders the prescriptive dose). So, too, the nuclear pharmacist has dispensed a number of radiotherapies, such as Indium-111 ibritumomab tiuexetan (Zevalin®) –the diagnostic dose required on the first approval of Zevalin to observe altered biodistribution of the Yttrium-90 Zevalin therapeutic dose (no longer required) and the Yttrium-90 Zevalin therapy; Iodine-131 tositumomab (Bexxar®) –radiotherapy discontinued, Strontium-89 chloride (Metastron™); Samarium-153 Lexidronam (Quadramet®) and the recently approved radiotherapy Radium-223 dichloride (Xofigo®). The safe handling of the radiotherapeutic product by the nuclear pharmacist has long been established.

The story regarding the use, or lack of use, of Zevalin appears to not be the issue. The real issue surrounds the growth of radiotherapeutics as part of the anti-cancer regime. The June 2016 FDA approval of Gallium-68 dotatate injection (NETSPOT™) for neuroendocrine tumor imaging should be followed on in the near future with the theranostic partner Lutetium-177 somatostatin analogue peptide (Lutathera). Lutetium-177, Actinium-225, Bismuth-213, Rhenium-188, Tin-117^{m} and other conjugates of Yttrium-90 and/or Samarium-153 could bring many new cancer therapies into the treatment regimes. The patient care and point of care quotient will call on consideration to have these therapies reach to far greater geographic areas for the point of service. We believe the teaming of the nuclear pharmacist and the specialty physician will satisfy the regulatory aspects in the safe handling of the alpha and beta radionuclides and can expand the geographic points of service ensuring quality patient care.

We urge the ACMUI on the T&E for alpha and beta emitters to examine the alternative solution proposed in this letter which could significantly improve patient point of care access to radiotherapeutic treatments in the hematology/oncology setting, while addressing important radiation safety considerations.

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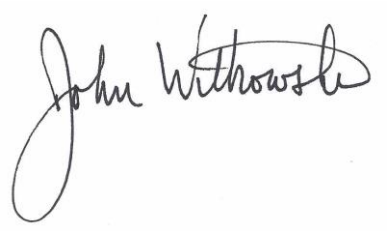
Thank you for considering the above comments, and please do not hesitate to contact John Witkowski, UPPI at 770-205-2651, with any questions concerning this letter.

Sincerely,



President
UPPI, LLC.