CHAIRMAN Resource

From: Mark Tulchinsky, MD <mtulchin@psu.edu>
Sent: Thursday, July 04, 2019 12:51 AM
To: CHAIRMAN Resource
Cc: Mark Tulchinsky; Lopas, Sarah
Subject: [External_Sender] Draft Approaches for Addressing Training and Experience Requirements for Radiopharmaceuticals Requiring a Written Directive, Section 10 CFR Part 35.390(b)

Honorable Kristine Svinicki, Chairman
U.S. Nuclear Regulatory Commission
Office of Administration
Mail Stop: TWFN–7–A60M
Washington, DC 20555–0001
ATTN: Program Management, Announcements, and Editing Staff
Re: Draft Approaches for Addressing Training and Experience Requirements for Radiopharmaceuticals Requiring a Written Directive, Section 10 CFR Part 35.390(b)

The Honorable Kristine Svinicki:

Thank you for seeking input on this timely and critical matter concerning a vitally important therapy option – therapeutic radiopharmaceuticals. Allow me to summarize the product of my extensive personal experience in general medicine and Nuclear Medicine as it relates to the above-referenced question the agency posed to the stakeholders.

The primary question posed to the NRC was "Whether it makes sense to establish tailored T&E requirements for different categories of radiopharmaceuticals" in order to broaden the Authorized User (AU) workforce in this country. I offer here forth a comprehensive deliberation, encompassing direct and indirect consequences of implementing the "tailored T&E", which is based on my hands-on work in the specialty field of Nuclear Medicine for the past 30 years and active participation in the National healthcare initiatives.

The direct goal of "tailored T&E" would be to create pathway(s) for credentialing novel AUs (NAUs), i.e. physicians from specialties other than the ones that traditionally contributed to the current AU workforce. The traditional AUs (TAUs) include Nuclear Medicine Physicians (NMPs), Radiologists (RADs) and Radiation Oncologists (ROs). Undoubtedly, the specialty of Oncology will be the dominant source of NAUs, but not the only one by any stretch of the imagination. Therefore, it is reasonable to deliberate the new paradigm of NAU's by considering that some Oncologists will be trained to become AUs and will be administering therapeutic radiopharmaceuticals (TRPs). The TRPs are the only agents that were implied in the above described "different categories of radiopharmaceuticals".

It is self-evident that all TRPs are by definition high-risk drugs as their administration caries a certain radiation exposure to a patient it is prescribed for, as well as the potential risk of radiation to the members of the public. The latter is especially relevant to their family members.

Allow me to complement the language of the Federal Register in order to characterize, as precisely and comprehensively as I can, the agents under the consideration in this Notice. Therapeutic Radiopharmaceuticals (TRPs) are agents that span a broad range of chemicals from simple salts like sodium iodide-131 to various complex organic molecules that contain a radioactive isotope. While a chemical agent is biologically and/or mechanically destined for delivery into the diseased tissue, it is a radioisotope that is responsible for depositing a cytocidal radiation injury that leads to the therapeutic effect of TRPs. By definition then TRPs are developed to inflict injury on the targeted tissues, but their use is invariably associated with a high likelihood of unintended injury to healthy tissues. Therefore, TRPs are tightly regulated by Federal and State agencies. In the post 9/11 World, we also must recognize the public danger posed by a potential for weaponizing TRPs by international and/or domestic terrorists. Any medically used radioactive materials, particularly the high activity contained in TRPs, could be weaponized into a radiologic dispersal device (RDD), a.k.a. a

"dirty bomb". The currently trained TAUs are well familiar with this danger that has been covered in our training and our literature. (1) It would be logical to presume that NAUs will have considerably less experience of handling high activities, as well as most of NAUs will be practicing in the community outpatient setting that a potential terrorist would have an easier time to target for illegally obtaining radioactive material to construct improvised explosive devices that contain stolen TRP products. As the new facilities receiving and administering those TRPs under the supervision of NAUs will be by definition less experienced, they would be at greater risk for allowing terrorists access to TRPs.

The tacit view of the oncologists and other physicians who would be considered for the NAU status is that current E&T requirements for achieving TAU status are too burdensome. This discussion obviously would not be necessary if oncologists and others would be eager and/or willing to obtain AU status through the traditional tracks approved by the Federal Statute. Those physicians who are seeking to become NAUs are currently the referring physicians, taking care of oncology patients with conditions that are targeted by the emerging TRPs. Currently, those same physicians would be the referring doctors sending their oncological patients to TAUs for consideration of radiopharmaceutical therapy. Hence, one important consideration is the implicit change of the current practice model of healthcare delivery where the referring physicians and the treating AUs serve patients' needs independently. This model provides a built-in mechanism of checks and balances.

Currently, a patient's pathway to an RPT-based treatment starts with a discussion of all treatment options with a primary doctor or an oncologist. If a patient selects RPT-based treatment option after discussing the pros and cons, the next phase of decision-making is a review of this option with an AU. The AU makes an independent decision regarding the appropriateness of the treatment option for a patient's condition and whether a patient is a good candidate for it from the perspective of an overall physical, mental and laboratory prerequisites. In my experience, there had been frequent instances when

a patient referred for a TRP was found unfit to proceed with such therapy by AU (myself). For example, not too long ago a patient with the poorly controlled psychiatric condition was referred for radioactive iodine therapy of hyperthyroidism. In my evaluation, the patient was unlikely to follow radiation precautions after therapy and I judged the patient to be better suited for thyroidectomy instead of radioactive iodine therapy. This avoided a risk of radiation exposure to unsuspecting members of the public from the patient who was highly unlikely to follow radiation precautions instructions. Another patient with metastatic prostate cancer was referred for bone pain palliation with TRP but on my (AU pre-therapy consult) evaluation was found to be in an advanced stage that conferred a dismal (less than a month expected survival) prognosis. A more appropriate for the circumstance pain management with oral medications was pursued instead and the patient had succumbed to the disease only 2 weeks later in comfort. Administration of TRP to this patient would have resulted in unlikely benefit during the remaining lifetime (usually takes up to 2 weeks to observe pain relief from TRP). This system of checks and balances will be circumvented by the introduction of NAUs who would likely also be the primary oncologist for the patient. This means that suboptimal or incorrect decision for using a TRP will be made more often under the "tailored T&E" system that obviates the mechanism of checks and balances through attaining consent and agreement for the same therapy from a treating independent AU.

I would like to reiterate that if a referring physician refers a patient that is poorly fit for therapy with a TRP, the treating AU has an obligation of checking on the appropriateness of the therapy indication and, if found to be invalid or even doubtful, raising and bringing this concern to the patient's and referring physician's attention. This mechanism of checks and balances is very important as it prevents unnecessary and treatments that could be too risky from happening. The proposed model will lead to the inevitable result of merging the referring physician and NAU into a single provider, which opens the possibility of practicing self-referral and would also remove the current built-in mechanism of checks and balances. The only result to be expected is overtreatments. It

is my understanding that self-referral has considerable challenges of compliance with the Federal regulatory stature and maybe indeed illegal as outlined in the Section 1877 of the Social Security Act (the Act) (42 U.S.C. 1395nn), a.k.a. the physician self-referral law that is commonly referred to as the "Stark Law". This law specifically refers to "physical therapy services" that would be pertinent to the matter at hand.

But even if this practice were legal through rulemaking that would exempt it, the dual role of an oncologist and the primary physician clinically taking care of a patient with malignancy and also being the NAU administering and supervising TRP administration would still be prone to abuse of overprescribing for the reason of the obvious financial incentive. The TRP management and administration is typically well reimbursed by CMS and other insurances and would be highly enticing to those who are able to both make a recommendation to a patient for using a TRP in the course of care and then supervise the administration of the same TRP. This practice would be similar to what is currently practices in regards to chemotherapy. Therefore, it would be important to review the practice of chemotherapy by oncologists as a prototype for what may happen with the practice of TRP by the same specialty and under the very similar regulatory and clinical circumstances.

The case that immediately comes to mind is an extreme example of chemotherapy abuse by an oncologist in the USA that was recently prosecuted. A Detroit area hematologist-oncologist was sentenced in 2015 to serve 45 years in prison for his role in a health care fraud scheme that included administering medically unnecessary infusions or injections to 553 individual patients and submitting to Medicare and private insurance companies approximately $34 million in fraudulent claims. (https://www.justice.gov/opa/pr/detroit-area-doctor-sentenced-45-years-prison-providing-medically-unnecessary-chemotherapy) It would be entirely conceivable that some of those unnecessary injections instead of chemotherapy could have been TRPs for some of the 553 victims if the novel pathway existed to allow this physician to gain AU status.

But this is not an individual one-off event. There is a building strong evidence in the medical literature that shows that financial gain is a clear driver of overuse of chemotherapy and other expensive and toxic drugs by oncological care providers. I refer you to the current literature for extensively documented evidence that supports it. (2-4) Starting the new pathway for NAUs could open a new floodgate to abuse and wasteful use of high-risk radioactive materials.

The original reason for requiring written directive for specific radiopharmaceuticals is that they pose the highest risk for developing severe health consequences for the subjects who receive it, as well as the public, in general, that would be exposed to the risk of external and internal exposure to radiation from the treated subjects. Since we are specifically addressing the radiopharmaceuticals given for therapy of cancer, it should be clear that those agents are of highest risk inherent in their purpose by design. Even in cases of isotopes that do not emit a long-range photon to permit for radiation exposure by external beam, it nevertheless leaves the internalization by contamination open to maintain the relatively high risk to the public. It is critical not to neglect the ever-increasing risk of terrorism that could take advantage of the more distributed supply of isotopes that allows for constituting plans for the creation of "dirty bombs".

The secondary question posed to the NRC was "how those categories should be determined (such as by risks posed by groups of radionuclides or by delivery method). All therapeutic radiopharmaceuticals are inherently high-risk and, therefore, categorizing into relatively more or less risky agents does not offer a reasonable solution to risk-mitigation. Indeed, the radiopharmaceuticals that appear to pose less risk because the radiation is contained in the target patient because of their short-range of the emitted photon actually should be viewed as much riskier from the perspective of ulterior use – such as the creation of dirty bombs.

Development of new E&T requirements is aimed at increasing numbers of AUs available to administer TRPs. This will consequently increase the

number of facilities that will be dispensing TRPs. The risk of medical events is proportional to the number of facilities and AUs. Thus, the number of medical events should be expected to increase proportionately. To the best of my understanding, the number of events is not related to the number of therapies performed but the sites of practice and the experience level of those sites. Widening the number of AUs is the intended purpose of this regulatory change. The number of less experienced AUs is an unavoidable consequence of this very same initiative. Increase in anticipated medical events, therefore, should be a logical outcome. This anticipated outcome is not acceptable without a convincing justification and I do not find such to be really present.

The number of practice sites involved in dispensing TRFs has other obvious consequences that have not been specifically queried by the NRC but warrant discussion in my opinion. The practice sites do get regularly inspected by the NRC or the State designated agency. Consequently, the governmental burden will be obviously increased proportionately. This without a doubt will require additional budget from the Federal and State governments. Such societal burden is not justified, in my opinion, and should be taken into consideration.

The above is sincerely submitted for your consideration,

Mark Tulchinsky, MD, FACNM, FSNMMI, CCD

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On Thu, May 23, 2019 at 9:05 AM Lopas, Sarah <Sarah.Lopas@nrc.gov> wrote:
Hi Dr. Tulchinsky,

In response to several requests from stakeholders (including SNMMI, ACR, and ASTRO) - we've extended the T&E comment period to July 3! That's a Wednesday. Here is the FRN that was published today announcing the extension of the comment period.... Draft Approaches for Addressing Training and Experience Requirements for Radiopharmaceuticals Requiring a Written Directive)

Experience Requirements for...

On May 2, 2019, the U.S. Nuclear Regulatory Commission (NRC) requested comments on draft approaches regarding th...

Just an FYI if you were planning on submitting comments. Still submit your comments via Regulations.gov – nothing has changed in that regard.

Regulations.gov

Thank you for your participation in our evaluation!

Sarah

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From: Lopas, Sarah
Sent: Thursday, May 02, 2019 12:32 PM
To: Mark Tulchinsky <mark.tulchinsky@gmail.com>
Subject: RE: training requirements review

Hi Dr. Tulchinsky,

I apologize for not following up with you sooner, but we have been very busy here working on the training and experience review and in fact, we just published a second *Federal Register* notice today that describes the draft approaches we've been considering for potential inclusion in the draft paper that we eventually have to write for our Commission. The Federal Register notice opens a short public comment period and announces two more public meetings. You may already be subscribed to our Medical List Server (and if you are not, you can see how to sign up here → Subscribe/Unsubscribe to Medical-Related Communications and Newsletter) – and a notice just went out via that, but I've copied that information below. Let me know if you have any questions or want to chat on the phone. But definitely submit your written comments before June 3 and if you can, listen in to one of the webinars noted below (I know that's tough though because they are in the middle of the work day).

Communications and Newsletter

Thank you,
Sarah

On May 2, 2019, the U.S. Nuclear Regulatory Commission (NRC) published a notice in the *Federal Register* announcing a 30-day public comment period and two public meetings on the NRC staff's draft approaches regarding the training and experience (T&E) requirements for administration of radiopharmaceuticals requiring a written directive. **The *Federal Register* notice can be accessed at: Draft Approaches for Addressing Training and Experience Requirements for Radiopharmaceuticals Requiring a Written Directive**

Experience Requirements for...

The U.S. Nuclear Regulatory Commission (NRC) would like input on draft approaches the staff has developed that w...

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The public comment period will end on June 3, 2019. Please follow the directions in the notice on how to submit written comments. The NRC is using the Federal rulemaking Web site, Regulations.gov

Regulations.gov

, to accept written comments on the docket (NRC-2018-0230).

The NRC will also be accepting oral comments during two public meetings scheduled for May 14, 2019 and May 23, 2019. The May 14 meeting will be open to members of the public for in-person attendance at the NRC's headquarters in Rockville, MD, and both meetings will be accessible for remote participation by moderated bridge line and webinar. The NRC's public meeting Web site will be updated with meeting details at least 10 days before the meetings: NRC: Public Meeting Schedule.

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To participate in the meetings via webinar and moderated bridge line, you must register in advance using the following URLs:

- Tuesday, May 14, 2019, 1:00 – 4:00 p.m.
  EDT: https://attendee.gotowebinar.com/register/26839476715014924

  Bridge Line: 888-452-5182
  Pass Code: 2649150

- Thursday, May 23, 2019, 10:00 a.m. – 12:00 p.m.
  EDT: https://attendee.gotowebinar.com/register/4099285410908048653

  Bridge Line: 888-452-5182
  Pass Code: 7476312

Additional information on the staff's T&E evaluation can be found at: NRC: Training and Experience (T&E) Evaluation

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If you have questions about the T&E evaluation or the public comment period and meetings, please contact Sarah Lopas at (301) 415-6360 or Sarah.Lopas@nrc.gov, or Maryann Ayoade at (301) 415-0862 or Maryann.Ayoade@nrc.gov.

From: Mark Tulchinsky [mailto:mark.tulchinsky@gmail.com]
Sent: Friday, March 15, 2019 10:59 AM
To: Lopas, Sarah <Sarah.Lopas@nrc.gov>
Subject: [External_Sender] training requirements review

Hello Sarah!

It was good to meet you and Maryann at the Orlando meeting earlier this year. I followed up with a detailed letter outlining my thoughts on the matter of training for AU licensure. Do you know where this all stands at the moment? Has NRC come up with any decision at this time? Feel free to call me today (the number below) as I am around and relatively free in the afternoon. I would appreciate hearing from you.

Respectfully,

Mark Tulchinsky, MD, FACNM, CCD

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