

# **Official Transcript of Proceedings**

## **NUCLEAR REGULATORY COMMISSION**

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on the Medical Uses of Isotopes

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UNITED STATES OF AMERICA  
NUCLEAR REGULATORY COMMISSION

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ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

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TELECONFERENCE

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MONDAY,

JULY 16, 2018

The meeting was convened via  
teleconference at 2:00 p.m., Christopher Palestro,  
ACMUI Chairman, presiding.

MEMBERS PRESENT:

CHRISTOPHER J. PALESTRO, M.D., Chairman

DARLENE F. METTER, M.D., Vice Chairman

PHILIP ALDERSON, M.D., Member

VASKEN DILSIZIAN, M.D., Member

RONALD D. ENNIS, M.D., Member

RICHARD L. GREEN, Member

MICHAEL D. O'HARA, Ph.D., Member

ZOUBIR OUHIB, Member

MICHAEL SHEETZ, Member

MEGAN L. SHOBER, Member

JOHN H. SUH, M.D., Member

LAURA M. WEIL, Member

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NON-VOTING MEMBERS:

MELISSA MARTIN

DESIGNATED FEDERAL OFFICIALS:

DOUG BOLLOCK, DFO

LISA DIMMICK, Alternate DFO

NRC STAFF PRESENT:

MARYANN AYOADE

VINCE HOLAHAN

SOPHIE HOLIDAY

ESTHER HOUSEMAN

KATIE TAPP

IRENE WU

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## P R O C E E D I N G S

2:00 p.m.

CHAIRMAN PALESTRO: All right, thank you.

Good afternoon and welcome to the Advisory Committee on Medical Uses of Isotopes for the comments on the draft SECY paper. My name is Dr. Christopher Palestro, and I am the Chair of the ACMUI.

Thank you all for attending the meeting.

And now I would like to turn it over to Mr. Doug Bollock, the Designated Federal Officer.

MR. BOLLOCK: Thank you, Dr. Palestro.

Good afternoon, everyone. As the Designated Federal Officer for this meeting, I'm pleased to welcome you to this public meeting of the Advisory Committee on the Medical Uses of Isotopes, or ACMUI.

My name is Doug Bollock, I'm Chief of the Medical Safety and Events Assessment Branch. I have been designated as the Federal Officer for this Advisory committee in accordance with 10 CFR Part 7.11. Present today is the Alternate Designated Federal Officer, Lisa Dimmick, who is also our Medical Radiation Safety Team Leader.

This is an announced meeting of the Committee being held in accordance with the rules and regulations of the Federal Advisory Committee Act and

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1 the Nuclear Regulatory Commission. This meeting is  
2 being transcribed by the NRC, and it may also be  
3 transcribed or recorded by others.

4 The meeting was announced in the June 7,  
5 2018 edition of the Federal Register, volume 83, page  
6 26503.

7 The function of the Committee is to  
8 advise the staff on issues and questions that arise  
9 on the medical use of byproduct materials. The  
10 Committee provides counsel to staff, but does not  
11 determine or direct the actual decisions of the staff  
12 or the Commission. The NRC solicits the views of the  
13 Committee and values their opinions.

14 I request that whenever possible, we try  
15 to reach a consensus on the various issues that we'll  
16 discuss today. And also recognize that there may be  
17 minority or dissenting opinions. If you have such  
18 opinions, please allow them to be read into the  
19 record.

20 At this point, I'd like perform a roll  
21 call of the ACMUI members participating today.

22 Dr. Christopher Palestro, Chairman.

23 CHAIRMAN PALESTRO: Here.

24 MR. BOLLOCK: Thank you. Dr. Darlene  
25 Metter, Vice Chairman.

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1 VICE CHAIRMAN METTER: Here.

2 MR. BOLLOCK: Thank you. Dr. Philip  
3 Alderson, Health Care Administrator.

4 MEMBER ALDERSON: Here.

5 MR. BOLLOCK: Thank you. Dr. Vasken  
6 Dilsizian, Nuclear Cardiologist.

7 MEMBER DILSIZIAN: Yeah.

8 MR. BOLLOCK: Thank you. Dr. Ronald  
9 Ennis, Radiation Oncology.

10 MEMBER ENNIS: Here.

11 MR. BOLLOCK: Mr. Richard Green, our  
12 Nuclear Pharmacist.

13 MEMBER GREEN: Here.

14 MR. BOLLOCK: Thank you. Dr. Michael  
15 O'Hara, our FDA Representative.

16 MEMBER O'HARA: Here.

17 MR. BOLLOCK: Thank you. Zouhir Ouhib,  
18 our Therapy Medical Physicist.

19 MEMBER OUHIB: Here.

20 MR. BOLLOCK: Thank you. Mr. Michael  
21 Sheetz, Radiation Safety Officer. Ms. Megan Shober,  
22 our Agreement State Representative.

23 MEMBER SHOBER: Here.

24 MR. BOLLOCK: Thank you. Dr. John Suh,  
25 Radiation Oncologist.

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1 MEMBER SUH: Here.

2 MR. BOLLOCK: Thank you. And Ms. Laura  
3 Weil, our Patients' Rights Advocate.

4 MEMBER WEIL: Here.

5 MR. BOLLOCK: Thank you. I confirm that  
6 we have quorum of over six members. On the phone,  
7 did we also have Ms. Melissa Martin?

8 MS. MARTIN: Yes, here.

9 MR. BOLLOCK: Thank you. And Mr. Robert  
10 Schleipman. Okay. Ms. Martin has been selected as  
11 the ACMUI Nuclear Medicine Physicist Representative.  
12 And Robert Schleipman has been selected as the ACMUI  
13 Health Care Administrator Representative. They are  
14 both pending security clearances, but may assist in  
15 the meeting. However, they do not have voting rights  
16 at this time.

17 I now ask the NRC staff members who are  
18 present to identify themselves. I'll start with the  
19 individuals who are in the room with me.

20 MS. WU: Irene Wu.

21 MS. TAPP: Katie Tapp.

22 MS. DIMMICK: Lisa Dimmick.

23 MS. HOUSEMAN: Esther Houseman.

24 MR. HOLAHAN: Vince Holahan.

25 MR. BOLLOCK: Okay, thank you. Now I'll

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1 go to NRC Headquarters employees who are on the phone.

2 MS. AYOADE: Maryann Ayoade.

3 MS. HOLIDAY: Sophie Holiday.

4 MR. BOLLOCK: Okay, thank you. Do we  
5 have any NRC regional employees on the phone? Okay.  
6 Members of the public who notified Ms. Ayoade that  
7 they would be participating in the teleconference  
8 will be captured in the transcripts.

9 Those of you who did not provide prior  
10 notification, please contact Ms. Ayoade at  
11 [maryann.ayoade@nrc.gov](mailto:maryann.ayoade@nrc.gov). That's M-A-R-Y-A-N-N dot A-  
12 Y-O-A-D-E at nrc.gov. Or (301)415-0862.

13 We have a bridge line available, and that  
14 phone number is (888)677-2595. The passcode to  
15 access the bridge line is 9887521, followed by the  
16 pound sign. This meeting is also using the GoTo  
17 webinar application to view presentation handouts  
18 real time.

19 You can access this by going to  
20 [www.gotowebinar.com](http://www.gotowebinar.com), that's www dot G-O-T-O-W-E-B-I-  
21 N-A-R dot C-O-M, and search in the meeting ID 419-  
22 602-667.

23 The purpose of this meeting is to discuss  
24 the draft report of the ACMUI Subcommittee on Training  
25 and Experience Required for All Modalities.

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1                   This report includes the Subcommittee's  
2           comments and recommendations on the NRC staff's  
3           evaluation of the training and experience  
4           requirements for different categories of  
5           radiopharmaceuticals in Title 10 of the Code of  
6           Federal Regulations, Part 35, medical use of  
7           byproduct materials, Subpart E unsealed byproduct  
8           material, written directive required.

9                   Individuals who'd like to ask a question  
10          or make a comment regarding a specific issue the  
11          Committee has discussed should request permission to  
12          be recognized by the ACMUI Chairperson, Dr.  
13          Christopher Palestro. Dr. Palestro, at his option,  
14          may entertain comments or questions from the members  
15          of the public who are participating with us today.

16                  Comments and questions are usually  
17          addressed by the Committee at the end of the  
18          presentation, after the Committee has fully discussed  
19          the topic. We ask that one person speak at a time,  
20          as this meeting is also close-captioned.

21                  I would also like to add that handouts  
22          and the agenda for this meeting are available on the  
23          NRC's public website. At this time, I ask that  
24          everyone on the call who is not speaking place their  
25          phones on mute. If you do not have the capability

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1 to mute your phone, please press star six to utilize  
2 the conference line mute and unmute functions.

3 I would ask everyone to exercise extreme  
4 care to make sure that the background noise is kept  
5 at a minimum, as any stray background sounds can be  
6 very disruptive on a conference call this large.

7 At this point, I would like to turn the  
8 meeting back over to Dr. Palestro.

9 MR. BOLLOCK: All right, thank you, Mr.  
10 Bollock. And at this point, I would like to turn the  
11 meeting over to Dr. Darlene Metter, who is the Chair  
12 of the Subcommittee on Training and Experience for  
13 All Modalities, and she will present the  
14 Subcommittee's evaluation of the draft SECY paper.  
15 Dr. Metter.

16 VICE CHAIRMAN METTER: Thank you, Dr.  
17 Palestro. And thank you for the introduction.  
18 Before I start, I'd like to thank my Subcommittee  
19 members, Dr. Philip Alderson, Dr. John Suh, Ms. Megan  
20 Shober, and Ms. Laura Weil for their contribution to  
21 this paper.

22 I'd also like to thank the opportunity to  
23 review and provide recommendations for the draft SECY  
24 paper entitled Staff Evaluation of Training and  
25 Experience Requirements for Administering

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1 Radiopharmaceuticals.

2 Now, as an introduction, I'd like to give  
3 the following. In June of 2015, because of  
4 stakeholder concerns that a shortage of AUs caused by  
5 the 700 hours of training and experience required to  
6 become an authorized user under Title 10, Code of  
7 Federal Regulations, 35.300, specifically 35.390,  
8 training for use of unsealed byproduct material, for  
9 which a written directive is required, was limiting  
10 patient access to therapeutic radiopharmaceuticals.

11 The ACMUI at that time formed a  
12 subcommittee to look into this matter. The charge  
13 of the subcommittee was to determine if the 700-hour  
14 training and experience requirement placed a hardship  
15 on patient access to alpha- and beta-emitting  
16 therapeutic radiopharmaceuticals.

17 And if necessary, to make recommendations  
18 for potential changes and establish recommendations  
19 for the total number of hours of training and  
20 experience for use of unsealed byproduct material for  
21 which a written directive is required.

22 The Subcommittee concluded that the  
23 current requirement of 700 hours' training and  
24 experience for authorized users did not adversely  
25 affect patient access to these radiopharmaceuticals,

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1 and that no change in the training and experience  
2 requirements was warranted.

3 The Subcommittee also noted that the  
4 current training and experience requirements had not  
5 been updated in nearly 15 years and recommended that  
6 in the future, periodic training and experience  
7 reviews be conducted.

8 This recommendation led to the creation  
9 of the Subcommittee on Training and Experience for  
10 All Modalities. This Subcommittee created a  
11 standardized template for training and experience  
12 reviews, which was completed for 10 CFR 35.100.  
13 However, due to ongoing patient access concerns, the  
14 Subcommittee was directed to expedite the review of  
15 10 CFR 35.300, specifically 10 CFR 35.390.

16 During the March 1, 2018 ACMUI  
17 teleconference meeting, the Training and Experience  
18 Subcommittee reported that two recent developments  
19 identified potential future problems with patient  
20 access to 10 CFR 35.300 for radiopharmaceuticals.

21 The first was a potential increase in  
22 therapeutic procedures related to the recent U.S. FDA  
23 approval for broad use of the therapeutic  
24 radiopharmaceutical lutetium-177 dotatate. The  
25 second was a continued decrease in the number of

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1 nuclear medicine physicians in training and sitting  
2 for the American Board of Nuclear Medicine initial  
3 certification exam.

4 Due to the potential future increase in  
5 the number of procedures and the concomitant decrease  
6 in AUs, the Subcommittee recommended that an  
7 alternate AU pathway should be reconsidered.

8 From this resulted a draft SECY paper,  
9 which I will summarize. This draft paper addresses  
10 the NRC staff initial recommendations based on  
11 limited stakeholder outreach for training and  
12 experience requirements for different categories of  
13 radiopharmaceuticals, with a specific focus on 10 CFR  
14 part 35 on the medical use of byproduct material,  
15 Subpart E, unsealed byproduct material, written  
16 directive required.

17 After the final re-revision of 10 CFR  
18 Part 35 in August 2017, the Commission tasked the NRC  
19 staff to evaluate the possibility of a limited AU  
20 training and experience pathway addressing the  
21 following. One, its feasibility for certain  
22 categories of radiopharmaceuticals.

23 Two, how to develop such categories.  
24 Three, the appropriate training and experience  
25 requirements for such categories. And four, whether

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1 the training and experience requirements should be  
2 based on hours or competency.

3 Under 10 CFR Part 35, Subpart E, the staff  
4 considered the possibility of an alternate limited AU  
5 pathway with tailored training and experience  
6 requirements for certain categories of  
7 radiopharmaceuticals. Options for such categories  
8 were considered, along with appropriate corresponding  
9 training and experience and the documentation of  
10 training competency.

11 More extensive stakeholder outreach is  
12 planned to address the feasibility of a limited AU  
13 status for training and experience requirements and  
14 competency assessment.

15 To evaluate the feasibility of a limited  
16 AU pathway, the NRC staff first determined the  
17 knowledge topic for a training and experience  
18 curriculum. The curriculum included the current  
19 training and experience categories in 10 CFR 35.390,  
20 which would then be tailored to the specific category  
21 of radiopharmaceuticals, with additional knowledge  
22 topics as needed.

23 The staff then solicited stakeholder  
24 input on three other topics. First, the fundamental  
25 and specific radiopharmaceutical knowledge required

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1 in 10 CFR 35.390 to safely administer the  
2 radiopharmaceuticals. The stakeholder response was  
3 overall support of the proposed knowledge topics.

4 The second was how to obtain this  
5 knowledge. The stakeholder response on this question  
6 was varied and ranged from maintaining the current  
7 training and experience, saying that only American  
8 Board of Radiology or American Board Nuclear Medicine  
9 certifications, competency assessments, and perhaps  
10 even radiopharmaceutical administration  
11 requirements.

12 The third question was how to evaluate  
13 the acquisition and independent application of this  
14 knowledge. The stakeholder response was varied but  
15 will likely require NRC and stakeholder collaboration  
16 to determine this assessment.

17 Other concerns were, one, categorizing  
18 radiopharmaceuticals, which had various stakeholder  
19 and NRC responses. Two, how to administer the  
20 training and experience requirements. And the staff  
21 was considering using the Reactor Operator Licensing  
22 Program as a, rather than a benchmark, but more as a  
23 guide to administer these requirements.

24 Three, NRC staff estimated that the  
25 required training experience would be up to 300

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1 classroom hours. Four, competency assessment method  
2 or methods would be an examination developed by the  
3 medical community, whether it be a written exam or a  
4 hybrid exam, with or without preceptor attestation,  
5 and potentially also forming a new specialty board.

6 The final conclusion that the staff made  
7 was it may be feasible to develop a limited AU pathway  
8 for certain categories of radiopharmaceuticals with  
9 a competency-based approach for tailored training and  
10 experience requirements and knowledge of skills  
11 assessment.

12 The ACMUI Subcommittee had several  
13 comments on the SECY paper. The first was that the  
14 ACMUI Training and Experience Subcommittee  
15 recommended that the development of an alternate  
16 pathway be reconsidered.

17 Two, the stakeholder outreach has been  
18 limited and was likely related to time constraints.  
19 Staff should consider a broader stakeholder outreach.  
20 But this outreach could assist in defining the  
21 categories for radiopharmaceutical for limited AU  
22 status, tailoring the limited T&E requirements, and  
23 assessing the success of the knowledge and skills  
24 obtained.

25 Third, collaboration with the medical

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1 community and other stakeholders to develop a  
2 competency-based assessment tool, mostly likely in  
3 advance, is commendable. Four, minimizing the  
4 training and experience requirements and thus one's  
5 knowledge and skills, potentially jeopardizes  
6 patients, personnel, and public safety.

7 Five, the initial projection of  
8 authorized users was underestimated in that only  
9 nuclear medicine physicians were considered. For the  
10 2017-2018 academic year, the total number of  
11 residents who could potentially meet the AU training  
12 and experience requirements in 10 CFR 35.390 is nearly  
13 900.

14 And this is a number that's all residents  
15 in training. And these are in radiation oncology,  
16 nuclear medicine, nuclear radiology, and the  
17 redesigned emerging Board of Radiology pathway.

18 The data on osteopathic AUs and on AUs  
19 leaving the workforce, however, is currently not  
20 available. Although this revised estimate of that  
21 total number of future AUs is encouraging, the  
22 Subcommittee still recommends reconsideration of an  
23 alternate AU pathway.

24 Number six. The Subcommittee is  
25 concerned about estimating the required training and

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1 experience classroom hours for an alternate pathway.  
2 Given that the curriculum for limited status AU has  
3 not been established, the Subcommittee feels that  
4 it's premature to address the issue of hours.

5 The Subcommittee feels strongly that  
6 should a decision be made to proceed with a limited  
7 AU status, the training and experience requirements  
8 must be based on the knowledge and skills necessary  
9 to maintain patient, personnel, and public safety,  
10 and not based on a predefined number of hours.

11 Given these comments, the Subcommittee  
12 has five recommendations. The first is that the  
13 ACMUI Training and Experience Subcommittee recommends  
14 reconsideration of the existing pathways to AU  
15 status.

16 This reconsideration should have the  
17 goals of first maintaining maximal safety for the  
18 patient, personnel, and the public. Second, maximize  
19 patient access to current and future  
20 radiopharmaceuticals. And thirdly, to clearly define  
21 the AU's scope of practice.

22 Second, the educational program must be  
23 all-inclusive for the limited AU status. The  
24 didactic component necessary to obtain limited AU  
25 status under 1035.390 must comprehensively cover the

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1 knowledge topics required for all AUs involved in 10  
2 CFR 35.300, thereby ensuring the safe use of  
3 radiopharmaceuticals for the patient, personnel, and  
4 the public.

5 Third, the assessment method or methods  
6 to assess AU competency must be objective and document  
7 both initial and continuing maintenance of competency  
8 for the limited AU status.

9 Fourthly, there should be greater and  
10 broader stakeholder input. And lastly, the NRC staff  
11 should conduct ongoing monitoring for potential AU  
12 shortages for 10 CFR 35.300. Data on the geographic  
13 distribution and practice patterns of AUs should be  
14 included in this surveillance.

15 So that's the end of our subcommittee  
16 report. Do I have any comments from the  
17 Subcommittee? Okay, hearing none, do I have any  
18 comments from the ACMUI Committee itself?

19 CHAIRMAN PALESTRO: Dr. Metter, this is  
20 Dr. Palestro. I have a question for you. First, the  
21 Subcommittee is to be commended for doing a more  
22 thorough investigation of the anticipated AUs that  
23 would be, quote unquote, graduating on a yearly basis.  
24 I think that's important information.

25 The Subcommittee's report says

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1 approximately 900 potentially could meet the  
2 requirements. How does that compare historically?  
3 What numbers have been meeting those requirements and  
4 obtaining AU status in the past? Is that, do you  
5 have that information?

6 VICE CHAIRMAN METTER: No, I don't have  
7 that information. I just looked at the current group  
8 of individuals that are in training at this point.  
9 We can look at that, you know, the past, though.

10 CHAIRMAN PALESTRO: Okay, that might help  
11 to give a better picture of what we potentially could  
12 expect in the future.

13 MEMBER SUH: Dr. Palestro, this is John  
14 Suh, I just want to make a quick comment regarding  
15 your question.

16 CHAIRMAN PALESTRO: Yes.

17 MEMBER SUH: So if you look at the  
18 historic data which is provided from the American  
19 Board of Radiology, in terms of radiation oncology  
20 residents, if you look at the year 2006-2007, there  
21 were 585 slots, and the vast majority of those being  
22 filled. And if you look at 2016-2017, there were 808  
23 slots, with the vast majority of those positions being  
24 filled.

25 So in the ten-year period, there is an

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1 increase of about 220 potential authorized users who  
2 would be radiation oncologists.

3 CHAIRMAN PALESTRO: Okay, thank you.  
4 But the numbers you give are the total enrolled in  
5 the program, which is, if I'm not mistaken, four  
6 years. So the number of graduates then would be, or  
7 new AUs, would be approximately 25% of that on an  
8 annual basis. Am I correct?

9 MEMBER SUH: Yes, it would be about 200.  
10 And the number of programs for that ten-year period  
11 has increased from 79 programs to 92 programs. So  
12 an increase of 13 programs over that decade.

13 CHAIRMAN PALESTRO: Do you anticipate any  
14 further increases in the number of programs?

15 MEMBER SUH: I do know some programs that  
16 will be applying for residency. I couldn't give you  
17 an exact number in terms of what that number would  
18 be.

19 CHAIRMAN PALESTRO: Thank you.

20 VICE CHAIRMAN METTER: Also there's a  
21 small number also in radiology with the increased  
22 number of individuals in the nuclear radiology and  
23 the new Board pathway for being an AU. And I have a  
24 number, this past or this year, I think there were 11  
25 graduates. And I think there's, that's just for this

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1 year.

2 Any other comments from the Committee?

3 MEMBER GREEN: Dr. Metter, this is  
4 Richard Green. I wish we had more clarity on the  
5 number of authorized users, the number of licensees.  
6 I mean, that's just something we don't have.

7 But I think it's a great opportunity to,  
8 although the historical hours and assessments of  
9 competency based on hours has been in place for 15  
10 years, no one can really say, you know, it's written  
11 in stone in a CFR.

12 But no one can really say what that was  
13 based upon, or whether those hour levels are  
14 appropriate today in today's modern modes of  
15 learning, computer-based training or web training.  
16 So I just think it's valuable that there's now a  
17 standing committee that you chair that looks at what  
18 is the current, really, the appropriate way to assess  
19 competency.

20 And I just think it's great that this is  
21 being refreshed now. So we can make comments  
22 relative to the request from the Commissioners and  
23 address the draft recommendations made by staff.

24 But to do that, we really take a look and  
25 see what it would take to adequately train a physician

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1 to safely administrate radiopharmaceuticals. Until  
2 that's done, we are looking at history, but not really  
3 knowing where it came from.

4 VICE CHAIRMAN METTER: Thank you. Are  
5 there any other comments from the Committee?

6 MEMBER OUHIB: Yes, Dr. Metter, this is  
7 Zoubir Ouhib. I think to answer Mr. Green's comment  
8 is that my understanding is really this is based on  
9 all the education that was basically required from an  
10 authorized user, you know.

11 And I guess if you go back and take a  
12 look at what these authorized users had to complete  
13 and so on, I think that it will be a reasonable  
14 estimate of that kind of a number, in my opinion.

15 VICE CHAIRMAN METTER: Okay, thank you.

16 MEMBER SHOBER: This is Megan Shober, I  
17 also have a comment about the hours.

18 VICE CHAIRMAN METTER: Yes.

19 MEMBER SHOBER: So when the 10 CFR 35 had  
20 its major revision the last time, the final rule was  
21 in 2002, the proposed rule was issued in 1998. And  
22 as part of that, and with the proposed rule, there's  
23 a pretty extensive discussion on where the number,  
24 the training and experience hours comes from.

25 There's about five pages of discussion

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1 about where that 700 hours comes from. So I encourage  
2 people to take a look at that original proposed rule  
3 from August 13, 1998. And it informs a lot of this  
4 discussion that we've been having over where the hours  
5 come from.

6 VICE CHAIRMAN METTER: Okay, thank you.  
7 Okay, are there any more comments from the ACMUI  
8 Committee members?

9 CHAIRMAN PALESTRO: Dr. Metter, this is  
10 Dr. Palestro again. In your summary of the draft  
11 SECY paper, you said it addresses the NRC staff's  
12 initial recommendations based on limited stakeholder  
13 outreach. Could you elaborate on what constituted  
14 the limited stakeholder outreach and what was the  
15 basis of selection of those stakeholders?

16 VICE CHAIRMAN METTER: As far as the  
17 stakeholders, I believe it was in the report.  
18 Maryann, or is there an NRC staff that can help with  
19 that?

20 MR. BOLLOCK: Yes, this is Doug Bollock,  
21 I can address that. So we had, I think, based on  
22 that paper, we had a limited time frame to get a  
23 limited amount of stakeholder outreach. And we are  
24 also limited by our burden requirements under OMB.  
25 So we can only reach out to nine non-federal agencies

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1 or non-federal entities.

2 So we made the determination of the nine.  
3 We wanted to get as broad of a spectrum as we could,  
4 so we asked a number of licensees, picked a couple of  
5 licensees from different parts of the country trying  
6 to get a large institution and maybe a smaller size  
7 institution that's represented.

8 We asked one of the, a professional  
9 society. We asked CORAR for, I guess manufacturing,  
10 I'm trying to think what the proper term is. But we  
11 asked one board, the American Board of Nuclear  
12 Medicine, and we also reached out to one of our co-  
13 regulators, we reached out to Virginia.

14 And then we did reach out to a number of  
15 federal facilities, Navy, the Army hospitals to get,  
16 to kind of increase the stakeholder, from licensees  
17 or from users of the radiopharmaceuticals.

18 We tried to get as broad of a, with the  
19 limits of only being able to ask nine non-federal  
20 entities, we tried to get as broad of a spectrum as  
21 we could with that limit. So with licensees, our  
22 board, professional organizations, and one state  
23 regulator.

24 VICE CHAIRMAN METTER: Thank you.

25 CHAIRMAN PALESTRO: Yeah, thank you, Mr.

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1 Bollock. That answers my question. I appreciate  
2 that.

3 VICE CHAIRMAN METTER: Are there any  
4 other questions from the ACMUI Committee or comments?

5 MEMBER OUHIB: Doctor Metter, this is  
6 Zoubir Ouhib again. I do have a comment, if you  
7 could go up a little bit on your document. Move to  
8 page one or two. There was a statement made  
9 regarding, let me just see that. I think this is  
10 relating to the FDA on the new isotope.

11 My question is that the, you know, there  
12 was a statement that says there's a potential increase  
13 of users or something. I'm just curious, that  
14 potential future increase is based on what, exactly?  
15 What data is used to actually make such a statement?

16 VICE CHAIRMAN METTER: Well, the dotatate  
17 has, it's going to be used for neuroendocrine tumors,  
18 and can be used for several of them. Most of the  
19 treatments right now with radiotherapy is limited,  
20 let's say for specific use. But this can be a broader  
21 use for neuroendocrine tumors.

22 Dr. Palestro, I believe you had looked  
23 into that in your report.

24 CHAIRMAN PALESTRO: Yes. The answer is  
25 that the previous radiopharmaceuticals that have been

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1 approved were approved with a, had very narrow  
2 approval. Typically, they were for patients who had  
3 failed all sorts of previous therapies and very  
4 specifically defined criteria.

5 Lutetium 177 dotatate, however, had a  
6 much broader approval, a much more general approval,  
7 and could be used conceivably at virtually any point  
8 during the patient's treatment. It could be used as  
9 a first line, it could be used a second line, it could  
10 be used as an endline treatment. Really up to the  
11 discretion of the individuals managing the patients.

12 And then in addition to that, these  
13 tumors, these gastro, entero, pancreatic,  
14 neuroendocrine tumors, which were once thought to be  
15 relatively uncommon, are now recognized to be the  
16 second most common GI tract malignancy. So that's  
17 how we came to the conclusion that the potential  
18 exists for a broader use of this agent than previous  
19 similar agents.

20 MEMBER OUHIB: And this is simply just  
21 an estimate here, is that correct?

22 CHAIRMAN PALESTRO: Correct.

23 MEMBER GREEN: Dr. Palestro, it's also  
24 an additional fact that a single patient with a  
25 gastro-entero-hepatic tumor would undergo multiple

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1 courses of radionuclide therapy also weighs into that  
2 consideration.

3 CHAIRMAN PALESTRO: To a lesser degree  
4 because patients who are being treated with radium  
5 dichloride also undergo multiple courses.

6 VICE CHAIRMAN METTER: Okay. Are there  
7 any additional comments from the ACMUI Committee  
8 members? Okay, I'd like to open the commentary then  
9 to the public.

10 OPERATOR: Thank you. Participants on  
11 the phone, if you have a comment at this time, press  
12 star one and record your name. One moment to see if  
13 we have any comments.

14 We have a comment from Sue, your line is  
15 now open.

16 MS. LANGHORST: Hi, this Sue Langhorst.  
17 Hi there. I had a few questions for the ACMUI and  
18 the NRC staff to consider.

19 My first question is will the NRC plan to  
20 track information on the kinds of physicians who  
21 utilize the specialty T&E training and experience  
22 tracks, as I'm terming them, and report back to the  
23 ACMUI the regulatory results and issues that come  
24 from this change, that is, how effective the training  
25 is for their regulatory compliance? That's my first

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1 question.

2 My next question is if new licenses are  
3 issued for this specialty track training and  
4 experience, who will function as the RSO?

5 And my third question is will authorized  
6 users with specialty track approval be able to be  
7 appointed as an RSO, and if so, what additional  
8 training will they be required to obtain? I thank  
9 you all for considering the questions.

10 MR. BOLLOCK: Thanks, Dr. Langhorst.  
11 This is Doug Bollock, I'm going to go kind of in  
12 reverse order to answer your questions. It's a  
13 little bit easier. So these are just the, so this  
14 is nothing set in stone yet, but we just thought of  
15 what are some other ways, what are possible ways to  
16 allow for expanded authorized users.

17 And one way is to have a limited  
18 authorized user, potentially, who would be limited to  
19 whatever drug that they were going to use. But a  
20 limited authorized user, we have not had any thought  
21 or taken into consideration of changing the  
22 requirements for an RSO.

23 Therefore, if we had an authorized, a  
24 limited authorized user and is just right now, again,  
25 we're just, we haven't planned on anything yet. But

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1 if they're I guess lesser requirements than a full,  
2 authorized user, it's unlikely that they would be,  
3 that they would meet the requirements for an RSO.  
4 Okay, so that likely they would not.

5 Your second question of who would  
6 function as an RSO, someone who is, meets the  
7 requirements for 35.50 and all the requirements in  
8 the license to be an RSO at whatever facility, or  
9 yeah, at a licensed facility. So those requirements  
10 are not, we're not considering any changes to the  
11 RSOs.

12 And then for your first question, I think  
13 we did, I don't think we quite understood your first  
14 question, and what. Were you asking if we, through  
15 our outreach, if we're going to get more information  
16 on the, on current AUs and their training or how they  
17 got training? I'm not, we're not sure we understand  
18 your first question, could you please repeat it?

19 MS. LANGHORST: Absolutely, absolutely.

20 MR. BOLLOCK: Thank you.

21 MS. LANGHORST: So really what, so Doug  
22 what I'm talking about is if the NRC and the ACMUI  
23 recommend that there be a specialty track, let's say  
24 like there is for 35.392 or 35.394 for I-131  
25 therapies. If there are different kinds of

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1 positions, then nuclear medicine and radiation  
2 oncology positions utilizing that track, will NRC be  
3 considering some way of reporting back any regulatory  
4 issues as far as what type of physician are having  
5 these issues?

6 And if that the training that's set for  
7 that level, is it adequate to meet all the regulatory  
8 compliance requirements? Not that I'm asking you to  
9 answer that question now, that's a question I'm  
10 suggesting you consider.

11 MR. BOLLOCK: Okay, thank you for the  
12 comment. We'll consider that.

13 MS. LANGHORST: Thank you all.

14 OPERATOR: Once again, if you have a  
15 question or comment, please press star one and record  
16 your name. Speakers, let me know whenever you're  
17 ready for the next question. And it looks like we  
18 have a question from Cindy Tomlinson. Your line is  
19 open.

20 MS. TOMLINSON: Thank you. Chairman  
21 Palestro and members of the ACMUI and NRC staff, thank  
22 you for allowing me to provide this statement on  
23 behalf of the American Society for Radiation  
24 Oncology.

25 In response to the ACMUI's comments on

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1 the draft SECY paper entitled Staff Evaluation of  
2 Training and Experience Requirements for  
3 Administering Radiopharmaceuticals being discussed  
4 today, because the draft SECY paper is not public,  
5 our comments reflect only on the ACMUI draft and  
6 report and recommendations.

7 As we have commented in past statements  
8 to the ACMUI, we strongly oppose any reduction in the  
9 training experience requirements found in 10 CFR  
10 35.390, training for use of unsealed byproduct  
11 material, for which a written directive is required.

12 ASTRO believes that the requirements  
13 found in this section are appropriate to protect the  
14 safety of patients, public, and practitioners and  
15 should not be changed. Radiopharmaceuticals are  
16 highly effective in treating cancer, with possible  
17 harmful effects to both the patient and the public if  
18 not used correctly and under the supervision of a  
19 highly trained physician.

20 The rigorous T&E requirement contributes  
21 to the excellent safety record of  
22 radiopharmaceuticals. We believe that it is  
23 important that the person administering the  
24 radiopharmaceutical is appropriately trained in the  
25 safe handling, exposure risks, and the management of

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1 side effects of radiation.

2 In general, ASTRO is comfortable with the  
3 broad recommendations made by ACMUI and believes that  
4 a thorough and comprehensive review of current T&E  
5 requirements is reasonable.

6 Additionally, we fully support the  
7 ACMUI's recommendation that the NRC conduct a  
8 thorough examination of geographic distribution and  
9 practice patterns of current AUs under 10 CFR 35.390  
10 and 300, as well as taking greater stakeholder input.

11 The American Board of Radiology estimates  
12 that between 2007 and 2017, approximately 1650  
13 radiation oncologists were certified by the ABR with  
14 an authorized user eligibility designation and may  
15 become AUs.

16 In addition, we estimate that there are  
17 approximately 2200 radiation oncology facilities in  
18 the US. Together with current radiation oncology  
19 AUs, the 773 radiation oncology residents currently  
20 in residency programs and nuclear medicine-trained  
21 AUs nationwide, there are likely enough AUs to  
22 administer radiopharmaceuticals.

23 We caution a change in the current  
24 requirements without a comprehensive investigation  
25 could result in unintended harm to patients,

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1 personnel, and the public. ASTRO looks forward to  
2 continuing to work with both the ACMUI and the NRC as  
3 we continue deliberations and review on this very  
4 important topic. Thank you.

5 VICE CHAIRMAN METTER: Thank you.

6 OPERATOR: Once again, if you have a  
7 question or comment, please press star one and record  
8 your name. It looks like we have a comment from Paul  
9 Wallner, your line is open.

10 MR. WALLNER: Thank you, good afternoon.  
11 My name is Dr. Paul Wallner, I'm a radiation  
12 oncologist who is separately Board-certified in  
13 radiation oncology and diagnostic radiology in  
14 nuclear medicine. I previously served as Chief of  
15 the Clinical Radiation Oncology Branch of the  
16 National Cancer Institute, when my research interest  
17 was in targeted radiopharmaceuticals.

18 I'm speaking today on behalf of the  
19 American College of Radiology, ACR. The ACR  
20 represents over 35,000 diagnostic radiologists,  
21 interventional radiologists, radiation oncologists,  
22 nuclear medicine physicians, and medical physicists.

23 The ACR understands the tight deadline  
24 and external pressures prompting the staff's draft  
25 paper. However, we strongly urge more extensive

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1 public engagement of the medical stakeholder  
2 community before the NRC takes any significant action  
3 on the issues covered by the draft paper.

4 Forward movement on this topic seems to  
5 be predicated on the presumption that the 700-hour  
6 training and experience requirements in 10 CFR 35.390  
7 is no longer appropriate, particularly for  
8 individuals without NRC-recognized Board  
9 certification.

10 But the underlying concerns have yet to  
11 be substantiated in a quantitative, impartial, and  
12 apolitical fashion. Before there is any serious  
13 movement towards modifying T&E content or hours,  
14 there should be a fact-driven assessment of the  
15 external criticisms regarding 35.390.

16 After all, 35.390 has a track record of  
17 success in providing NRC with a reasonable assurance  
18 of the adequate protection of public health and  
19 safety. To help substantiate or disprove AU  
20 population concerns, it's most important for NRC to  
21 gather trustworthy data on the active AU population  
22 providing various therapies under 35.390.

23 The collective data should enable  
24 exploration of AU numbers and coverage over a multi-  
25 year period of time. This suggestion has been made

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1 previously, and we understand that such an activity  
2 would be labor-intensive and require collaboration  
3 with agreement states and broad scope licensees.

4 However, without confirmation by NRC of  
5 a problem, there is a questionable technical basis  
6 for any rulemaking to modify 35.390 or the other  
7 subparts of Part 35.

8 Moreover, any presumption of a future AU  
9 shortage informed solely by ABNM trends neglects the  
10 radiation oncology and new nuclear radiology  
11 pathways, which we understand to be stable, or in the  
12 case of nuclear radiology, expanding in size and  
13 distribution.

14 While prescriptive, the 700-hour training  
15 and experience prerequisite in 35.390 was  
16 fundamentally intended to ensure prospective AUs,  
17 without certification from the NRC-recognized board,  
18 have an adequate base of knowledge and radiation  
19 safety to supervise the proper use of these  
20 therapeutical medical nuclear materials, including  
21 medical event prevention, identification, and  
22 mitigation.

23 If NRC determines, based on data, that a  
24 rulemaking to overhaul 35.390 T&E requirements is  
25 ultimately necessary, any future regulatory

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1 modification must reasonably ensure that clinicians  
2 who do not possess the expertise obtained via their  
3 residency programs and fellowships can appropriately  
4 fulfill AU responsibilities and protect their  
5 patients, staff, and other members of the public.

6 In conclusion, the ACR supports more  
7 extensive engagement of medical stakeholders on  
8 issues discussed in the draft paper. We look forward  
9 to seeing the final product at the end of summer and  
10 hope it reflects both the needs for more public  
11 engagement, as well as the need for an NRC assessment  
12 of AU members to justify any further action.

13 The ACR also hopes to provide input to  
14 the ACMUI on its own efforts related to these issues.  
15 Thank you for your time.

16 VICE CHAIRMAN METTER: Thank you, Dr.  
17 Wallner. Are there any other --

18 OPERATOR: We have a question. Yes, we  
19 do have an additional question. It comes from  
20 Bennett Greenspan. Your line is open.

21 MR. GREENSPAN: Hello, thank you. I'm  
22 Dr. Bennett Greenspan, I'm a nuclear medicine  
23 physician and radiologist and the immediate past  
24 President of the Society of Nuclear Medicine and  
25 Molecular Imaging. And I have a few brief comments.

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1 I pretty much agree with, I shouldn't say  
2 pretty much, I agree with the ACMUI's Subcommittee  
3 report. I did want to point out that physicians who  
4 don't know what they're doing could create severe  
5 harm to patients, and even personnel in the public,  
6 if they're not careful and so on.

7 And so physicians completing an alternate  
8 pathway must have the knowledge and basic science and  
9 clinical information to the same degree as those  
10 people trained in nuclear medicine, radiology, or  
11 radiation oncology.

12 And it also turns out that to do these  
13 therapies properly, these physicians need to have  
14 some background in understanding the imaging related  
15 to these therapies for optimal patient care.

16 And one other point I'd like to mention  
17 is that physicians in nuclear medicine, nuclear  
18 radiology, and radiation oncology training programs  
19 are now, it's supposed to be related information but  
20 it immersed it during their training. They're  
21 basically involved in this for several years during  
22 their training.

23 And other physicians such as medical  
24 oncologists do not have this training at all. And  
25 so they would, they were just totally deficient in

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1 anything related to radiation physics, radiation  
2 safety, and so on. So you know, if they wish to do  
3 these therapies, they really need to have the same  
4 kind of knowledge and skills that nuclear medicine,  
5 nuclear radiology, and radiation oncology physicians  
6 have.

7 I did want to point out that the number  
8 trainees in nuclear medicine appears to have  
9 stabilized over the last couple of years.

10 And one other comment, the future of  
11 these therapies I think will probably include  
12 combinations of various alpha and beta emitters. And  
13 so it's going to get much more complicated, and it's  
14 going to take some real expertise in the physicians  
15 providing these therapies. Thank you very much.

16 OPERATOR: Back to you, speakers. I'm  
17 showing no other comments at this time.

18 VICE CHAIRMAN METTER: Okay. So if there  
19 are no other comments, the Subcommittee, this  
20 committee, or its public, I turn this over back to  
21 Dr. Palestro.

22 CHAIRMAN PALESTRO: All right, thank you,  
23 Dr. Metter. I do have one final comment. I do want  
24 to point out that no one on the ACMUI, the  
25 Subcommittee, or staff has suggested anything about

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1 minimizing or fast-tracking or limiting training and  
2 experience requirements. And that's certainly not  
3 the intention of, and I'll take the liberty of the  
4 speaking for the Subcommittee, the ACMUI and the  
5 staff.

6 And in fact, I would call your attention  
7 to the last page of the Subcommittee's report. At  
8 the top of the page, item number four, minimizing the  
9 training and experience requirements and thus one's  
10 knowledge and skill potentially jeopardizes patient,  
11 personnel, and public safety. And that deserves re-  
12 emphasis. And I will conclude my comments there.

13 Any other comments from the Subcommittee,  
14 or the ACMUI?

15 OPERATOR: Excuse me, speakers, it looks  
16 like we have a few additional questions queueing up.  
17 Would you like to take those questions?

18 CHAIRMAN PALESTRO: Yes.

19 OPERATOR: Thank you. And it looks like  
20 we have a question from Michael Guastella. Your line  
21 is open.

22 MR. GUASTELLA: Thank you, and I'm sorry  
23 for signaling in there a little bit late, I apologize.  
24 I'm Michael Guastella, I'm the Executive Director of  
25 CORAR. Mr. Bollock mentioned a little bit earlier

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1       that we were one of the organizations that provided  
2       feedback.

3               And I'd just like to say that first of  
4       all, CORAR supports the ACMUI recommendation for the  
5       reconsideration of the existing pathways for AU  
6       status. And the goal, maintaining maximal safety for  
7       the patient, personnel, and the public, maximizing  
8       patient access to current and future  
9       radiopharmaceuticals, and clearly delineating the  
10      AU's scope of practice.

11             We've also supported in the past an  
12      alternative pathway and an alternative to the current  
13      700 hours' training and experience requirements under  
14      35.390. We have recommended a very specific scope  
15      of training requirements for radioisotope handling  
16      and radiation safety.

17             For specialists, like Hem/Oncs and  
18      medical oncologists, who wish to administer IV  
19      therapeutic radiopharmaceuticals, alpha- and beta-  
20      emitting radioisotopes, as has been mentioned, which  
21      have been prepared by a licensed nuclear pharmacist  
22      in a state-licensed radiopharmacy and dispensed to  
23      physicians as patient-ready doses.

24             In determining the appropriate amount of  
25      time and scope of content for radioisotope handling

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1 and radiation safety training that physician must  
2 have to safely administer these types of therapeutic  
3 drugs, CORAR has offered the following for ACMUI  
4 consideration.

5 And I reiterate, the limited role in  
6 handling these radio-labeled therapeutic drugs that  
7 are dispensed and delivered to physicians in patient-  
8 ready doses from licensed radio pharmacies. The  
9 radiological safety profiles and radiopharmaceuticals  
10 containing alpha- and beta-emitting isotopes. And  
11 physician experience in training and handling toxic  
12 non-radioactive therapies, such as cytotoxic  
13 chemotherapy agents.

14 In closing, I'd like to say the goal of  
15 the training experience requirements under an  
16 alternate pathway is to provide licensed medical  
17 specialists with competency and cognitive and  
18 psychomotor skills necessary to effectively and  
19 safely prescribe and administer specific  
20 radiopharmaceuticals. Thank you.

21 OPERATOR: It looks like we have two  
22 additional comments. The next one comes from Shaemus  
23 Gleason. Your line is open.

24 MR. GLEASON: Hi, and thanks for taking  
25 my question today. I'm Shaemus Gleason with Bayer

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1 Healthcare.

2 And in support of the ACMUI findings, we  
3 actually presented a petition of sorts to the degree  
4 of outlining some of the research that was missing  
5 around access to our drugs, particularly Xofigo.

6 And what you'll see is after five years  
7 on the market, 20,000 patients treated, 1400 sites up  
8 and running, we still notice significant patient  
9 falloff based on availability, both regionally and  
10 just generally.

11 And in addition to that, we see a number  
12 that exist that shows patients unwilling to travel  
13 that results in them not receiving the therapy. So  
14 once again, you know, we are very supportive of the  
15 ACMUI's recent attention to these issues, and look  
16 forward to engaging in further conversation. Thank  
17 you.

18 OPERATOR: We have a question from  
19 Bennett Greenspan. Your line is open.

20 MR. GREENSPAN: Thank you. This is  
21 Bennett Greenspan again. Again, I'm a nuclear  
22 medicine physician and radiologist. I'm the  
23 immediate past President of the Society of Nuclear  
24 Medicine and Molecular Imaging.

25 We were, we the Society of Nuclear

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1 Medicine and Molecular Imaging, were expecting to  
2 have a statement, and that hasn't been presented. So  
3 if you don't mind, I'd like to present it on behalf  
4 of the Chair of the Government Relations Committee.  
5 I am a member of that committee, and we the Society,  
6 appreciate the opportunity to address the ACMUI on  
7 this topic.

8 SNMMI, together with representatives from  
9 the American College of Nuclear Medicine, the ACNM,  
10 and the American Society of Radiation Oncology, ASTRO  
11 --

12 VICE CHAIRMAN METTER: Did we lose Dr.  
13 Greenspan?

14 CHAIRMAN PALESTRO: I don't hear him on  
15 the line.

16 OPERATOR: He'll need to redial back in,  
17 or press star and one. It looks like we've lost him.

18 CHAIRMAN PALESTRO: All right, let's give  
19 him a couple of moments, see if he can rejoin the  
20 meeting.

21 MR. BOLLOCK: And this is Doug Bollock.  
22 We did receive, as you know we received a letter from  
23 SNMMI, ACNM, and ASTRO combined. We also received  
24 one from Bayer. Yeah, those will be publically  
25 available when we post the transcripts for this

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1 meeting.

2 So Dr. Greenspan, if you hear us, your,  
3 the combined statement from SNMMI, ASTRO, and ACNM  
4 will be publically available. It has been received  
5 by ACMUI and the NRC, so we do have that, we are  
6 aware. And the rest of the public will be able to  
7 see it when the transcripts and everything else from  
8 this meeting are shared.

9 CHAIRMAN PALESTRO: All right, thank you,  
10 Mr. Bollock. Are there any other comments or  
11 questions from the Subcommittee, the ACMUI, or the  
12 public?

13 OPERATOR: We do have an additional  
14 question from the public. We have a follow-up  
15 question from Michael. Your line is open, Michael.

16 MR. GUASTELLA: Thank you. This is  
17 Michael Guastella again. And I guess my question is  
18 more of a process question. So I realize that the  
19 draft report has been presented the ACMUI. It's been  
20 reviewed. Maybe Mr. Bollock can speak to what the  
21 next step would be. I believe he said in March that  
22 the final report, the NRC staff report, is due to the  
23 Commission late summer.

24 I may have, my recollection may not be  
25 accurate. I'm just kind of curious if he could

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1 comment or anyone can comment on that. And will this  
2 require changes to rulemaking, or are there other  
3 pathways that an alternate pathway could be  
4 considered? Thank you.

5 MR. BOLLOCK: Thanks for that question,  
6 this is Doug Bollock again. So we owe the Commission  
7 a, or we owe a product to the Commission on August  
8 31, and so it'll be delivered to the Commission August  
9 31 and made public within a few days of that.

10 So it will be available to the public I  
11 would say probably the first week in September.  
12 Yeah, subject to Commission, they get a chance to  
13 look at it and then it is made public after that  
14 point.

15 OPERATOR: Thank you, speakers. Once  
16 again, if you'd like to ask a question or a comment,  
17 please press star then one. We have a question from  
18 Carol Marcus. Your line is open.

19 MS. MARCUS: Thank you very much, Dr.  
20 Palestro and members of the ACMUI. I am opposed to  
21 an alternate pathway. I urge the ACMUI to follow the  
22 money here. The radiopharmaceutical companies want  
23 to sell more drugs. The medical oncologists who  
24 would not order Zevalin on their patients because  
25 they couldn't make money on it now want to get

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1 licenses so they can make money on it.

2 This patient access issue I think is  
3 really a nonexistent issue. I think it's more a  
4 money issue.

5 The NRC is jumping on this because by  
6 selling more licenses, it's going to make a lot more  
7 user fee money to support its medical program  
8 bureaucracy. And so I think that you really have to  
9 look at the money.

10 If somebody living in Podunk, USA needs  
11 a triple CABG, he's not going to get it at his little  
12 25-bed community hospital or county hospital where he  
13 lives. He is going to have to travel. Because  
14 complex medical procedures are not available all over  
15 the United States anywhere you live. And people are  
16 used to that fact.

17 Now, there's no limit to how low the  
18 quality of medicine can get, but that doesn't mean  
19 it's a good idea. I think these people who need  
20 specialized nuclear medicine therapy, which is  
21 combined with imaging, as I think Bennett Greenspan  
22 mentioned, or somebody mentioned, more and more  
23 combined. The whole reason lutetium is used for  
24 therapy is that it allows imaging as well as the  
25 therapy of the beta particle.

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1                   So you need even more qualified and  
2           competent and experienced and knowledgeable  
3           physicians for these therapies than you used to.  
4           This is no time to degrade the training and  
5           experience. We need the highly skilled  
6           practitioners.

7                   Back in 1994, the ACMUI unanimously voted  
8           to get rid of the 80-hour program for endocrinology,  
9           on the basis that they simply do not get the education  
10          and training in all the aspects of physics, radiation  
11          safety, and more modern nuclear medicine requirements  
12          than they did back in 1946 when that 80-hour program  
13          started.

14                  But the NRC ignored the ACMUI completely.  
15          This was the recommendation for the 1995, 1997 I guess  
16          it was, redo of all of Part 35. So when physicians  
17          in non-nuclear medicine or radiology practices say  
18          they want an 80-hour program as well, I think we  
19          should say that doesn't work. Albert Einstein  
20          couldn't learn this stuff in 80 hours, let alone  
21          somebody with no basic training in radiology or  
22          nuclear medicine.

23                  And just bear in mind follow the money  
24          and let's stick with the qualifications that we've  
25          got. And I would add I would like to see the NRC

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1       enforce them. I have seen the NRC examine residency  
2       training programs to see where the 200 and 500 hours  
3       are. And I think a lot of people's programs really  
4       don't reflect that. And I think it needs  
5       enforcement.

6               I got a letter from the head of NMSS a  
7       few weeks ago commenting on a letter I had sent, who  
8       insisted that the NRC does examine this. And I had  
9       to write back and tell him you're really under a  
10      misconception. NRC does not look at these hourly  
11      trainings.

12             And the preceptor statement has nothing  
13      to do with ascertaining those training hours either.  
14      And in this morning's Federal Register the NRC has  
15      announced among other things that the preceptor  
16      requirement is gone as of, you know, mid-January.

17             So without that last-ditch preceptor  
18      attestation of confidence, you really better make  
19      sure that the hourly and content requirements of the  
20      residency training programs are being met. And I  
21      really think that in many residency training programs  
22      they are not. Thank you very much.

23             VICE CHAIRMAN METTER: Thank you. Did  
24      Dr. Greenspan get back on?

25             OPERATOR: Again, Michael, if you're on

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1 the line, please press star one to ask a question or  
2 finish your statement. One moment to see if he joins.

3 VICE CHAIRMAN METTER: Thank you.

4 MR. BOLLOCK: Dr. Palestro, this is Doug  
5 Bollock, and if I may, we appreciate the comments  
6 from everyone, including Dr. Marcus. I just want to  
7 clarify, one clarification to Dr. Marcus's statements  
8 to the Part 35 rule that went out. The preceptor  
9 attestation removal was only for Board-certified AUs.  
10 That's just a clarification.

11 CHAIRMAN PALESTRO: Thank you, Mr.  
12 Bollock. Any additional questions or comments?

13 MS. MARTIN: This is Melissa Martin. I  
14 am the incoming nuclear medicine member of the ACMUI.

15 Having served as Radiation Safety Officer  
16 at multiple medical centers in Southern California,  
17 I think one area that has not been considered that  
18 I'm not sure how we go about it, but when you raise  
19 the possibility that isotopes are going to come into  
20 medical facilities being sold or delivered directly  
21 to physicians, that will violate most of the  
22 hospital's radioactive materials licenses. Because  
23 right now, everything has to be delivered to a  
24 designated point.

25 I think the other thing we have to figure

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1 out is if they are now going to be delivered to a  
2 nuclear medicine department or a radiation oncology  
3 department, that staff's time is now going to be spent  
4 taking care of a physician for which they will re-  
5 coop none of the cost of their time to receive the  
6 isotope, prep the isotope, potentially clean up the  
7 mess of the isotope.

8 I just want those points to be  
9 considered, because I think the practical end of  
10 opening the range of users could be quite significant.

11 CHAIRMAN PALESTRO: Thank you for that  
12 comment. Any other comments?

13 OPERATOR: No questions from the phone.

14 CHAIRMAN PALESTRO: All right. In view  
15 of that, I'm going to ask if there is a motion to  
16 endorse the Subcommittee's report as written.

17 MEMBER ALDERSON: So moved. This is  
18 Alderson, so moved.

19 CHAIRMAN PALESTRO: Okay, thank you, Dr.  
20 Alderson. Second?

21 MEMBER SHEETZ: Second from Sheetz.

22 CHAIRMAN PALESTRO: Thank you. All in  
23 favor?

24 (Chorus of ayes.)

25 CHAIRMAN PALESTRO: Any opposed? All

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1 right, then the motion to endorse the report as  
2 written is unanimously passed. And at this point, I  
3 thank all of the participants, the Subcommittee for  
4 their work, the staff, the ACMUI, as well as the  
5 individuals who took time out of their day to comment  
6 on the bridge line.

7 And at this point, I will turn the meeting  
8 over to Mr. Doug Bollock.

9 MR. BOLLOCK: Thank you, Dr. Palestro.  
10 Just as a reminder to you all, the next ACMUI public  
11 meeting is our fall meeting here in NRC Headquarters  
12 in Rockville, MD, September 20 and 21.

13 And I'd like to thank ACMUI, the  
14 Subcommittee for reviewing our paper and providing us  
15 your comments and recommendations for full Committee,  
16 for your time today reviewing it and giving comments  
17 and considering it.

18 And also I'd like to thank all the public  
19 members who listened in today and gave comments. We  
20 appreciate it greatly.

21 OPERATOR: Thanks for your participation  
22 and you may disconnect at this time.

23 CHAIRMAN PALESTRO: Thanks a lot.

24 (Whereupon, the above-entitled matter  
25 went off the record at 3:08 p.m.)

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July 10, 2018

Douglas Bollock  
U.S. Nuclear Regulatory Commission  
Mail Stop 0-16G4  
Washington, DC 20555-0001

**Re: Statement on training and experience for authorized users: Guidance for the Nuclear Regulatory Commission (NRC) Advisory Committee on the Medical Use of Isotopes (ACMUI)**

Dear Mr. Bollock:

The leadership of the Society of Nuclear Medicine and Molecular Imaging (SNMMI), together with representatives from the American College of Nuclear Medicine (ACNM) and American Society of Radiation Oncology (ASTRO) formed an ad-hoc committee to offer their collective recommendation for potential updates to the 10 CFR 35.390, *Training for use of unsealed byproduct material for which a written directive is required*. We are offering suggestions specifically regarding the basic and clinical knowledge and skills needed for those seeking authorized user status through the “alternate pathway” (10 CFR 35.390(b)) to utilize radioisotopes to provide safe and effective clinical diagnostic and therapeutic results to patients.

With regard to training and experience requirements and the initial determination of competency, it is our opinion that mastery of the curriculum listed below will ensure high quality practice of radionuclide therapy. This didactic instruction and laboratory training is important for safe and effective therapies and should not be minimized. The use of unsealed sources for therapeutic applications is complex and has serious medical and safety risk associated with it, not only for the patient but for their family, and the public at large. As such, we feel it is important to maintain this high quality of training and experience.

Furthermore, we do not have evidence of an authorized user shortage, and there is no hard data to support a potential shortage. Because of broad licensing by the NRC, exact numbers of authorized users across various disciplines is difficult, if not impossible to obtain. While the number of nuclear medicine trainees have declined over the past few years, combined diagnostic radiology and nuclear medicine residencies have developed and are rapidly gaining in popularity, balancing the decline of nuclear medicine residency trainees. Furthermore, thousands of radiation oncologists are authorized users of unsealed source radiotherapies or have an authorized user eligibility specified on their American Board of Radiology (ABR) diploma. In addition, the pipeline of radiation oncologists is strong with 773 currently in residency programs. Of note, this is the same conclusion that was reached in the Statement by the American Society for Radiation Oncology (ASTRO) to the Advisory Committee on the Medical Use of Isotopes (ACMUI) on 3/1/2018.

Given the many authorized users currently available to perform these therapies, it is not surprising that delay in availability of these therapies to patients is rare. This can be seen across many types of radioisotope therapies such as I-131, Ra-223, I-131 ibritumomab, and Strontium-89. It is possible that there is a patient access issue to certain radioisotope therapies, which could be as a result of physician preferences or multiple other causes, but a shortage of authorized users does not appear to be one of them. An example of this is the current availability of Lu-177-Dotatate. Long wait lists at most institutions are due to the ramping up of this therapy at hospitals around the country, primarily due to the complexity of providing the therapy, availability of infusion spaces, and nursing support, but not due to a lack of authorized users available to administer the therapy.

As such, the availability of authorized treating physicians is not a valid reason to consider shortening the training and experience requirements for unsealed radioisotope therapy under 10 CFR 35.390(b). And, indeed, the complexity of the Lu-177-Dotatate therapy further highlights the need for rigorous training.

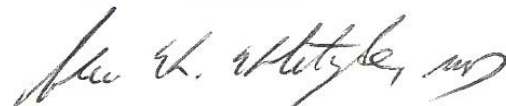
Detailed in the addendum to this letter is a description of the basic science and clinical training requirements that are necessary for the proper training of an authorized user. It also fully describes the initial certification of competency as well as maintenance of certification. We would like to stress that these training requirements/hours alone are not sufficient. For example, the three mandated experiences for a given therapy are not sufficient by themselves, but rather should be the culmination of many more such experiences in residency and in practice over several years.

Based on the above points, we oppose lowering the training requirements as currently stated in 10 CFR 35.390(b). We thank the ACMUI for the opportunity to provide input and look forward to future discussions.

Sincerely,



Bennett Greenspan, MD  
SNMMI Immediate Past-President



Alan Klitzke, MD, FACNM  
ACNM President



Laura I. Thevenot  
CEO, ASTRO

Cc: Christopher Palestro, MD, Chair, ACMUI  
Darlene Metter, MD, Vice Chair, ACMUI

**Addendum to SNMMI statement on training and experience for authorized users: Guidance for the NRC's ACMUI.**

The following are the basic science and clinical training and experience we feel are necessary to have as part of the total training designated in 10 CFR 35.390(b). Below that are the initial competency and maintenance of competency methods we feel are valid.

**Basic Science**

- Basic radionuclide handling techniques applicable to the medical use of unsealed byproduct material and radionuclides requiring a written directive. Ordering and receiving radiopharmaceuticals.
- Radiation physics: structure of matter, modes of radioactive decay, particle and photon emissions, half-lives and energies. Calculations of radioactive decay. Interactions of radiation with matter, principles of radiation detection, radiation units.
- Mathematics pertaining to the use and measurement of radioactivity, including decay calculations and calculations of organ and whole body dose. Statistics and medical decision making.
- Biochemistry, molecular biology and pharmacology.
- Chemistry of radioactive material for medical use, including: reactor, cyclotron and generator production of radionuclides, radiochemistry, formulation of radiopharmaceuticals.
- Radiation biology: biological effects of ionizing radiation. RBE. Radiation exposure. Radiation biochemistry. Radiation syndromes - Classification of radiation damage. Factors affecting radiation injury. Late effects. Low dose and low dose rate effects. Comparison of risk.
- Instrumentation: Principles of instrumentation used in detection, measurement, and imaging of radioactivity with special emphasis on gamma cameras, including single photon emission computed tomography (SPECT), SPECT/computed tomography (CT), positron emission tomography (PET), and PET/CT systems, and associated electronic instrumentation and computers employed in image production and display. Dose calibrators and survey instruments, including personnel monitoring equipment. Dosage and dose measurements. Quality control of instrumentation – QI, QA, QC, acceptance testing. Artifacts.
- Radionuclide production and quality control. Radiopharmaceutical QC. Radiopharmacology. Radiopharmacy. Surveys and monitoring techniques.
- Radiopharmaceuticals involved in radionuclide therapy and related imaging – biodistribution, mechanisms of localization, potential toxicity. I-131 sodium, Ra-223 dichloride, Sr-89 chloride, Sm-153 EDTMP, Y-90 microspheres, labeled antibodies, Lu-177 Dotatate, Lu-177 PSMA, other alpha and beta-emitting agents.
- Radiation protection, including units, means of reducing radiation exposure, Occupational and public radiation dose limits, shielding and personnel protective equipment (e.g., eye protection, syringe shields). Management of contamination, including spills. Evaluation of patients exposed to potentially dangerous levels of radiation, assisting in the medical management of persons exposed to ionizing radiation, management and disposal of radioactive substances, radiation accident management, and management of radiation safety programs in accordance with federal and state regulations.
- Demonstrate compliance with radiation safety rules and regulations, including Nuclear Regulatory Commission (NRC) or agreement state rules, local regulations, and the ALARA (as low as reasonably

achievable) principle for radiation protection. NRC – 10 CFR 19, 20, 35, especially 10 CFR 35.390.

Requirements for training and record keeping. National and international agencies. Restricted and non-restricted areas. Radionuclide therapy written directive. Patient release criteria.

- Medical events – determination of occurrence, evaluation of cause(s) and consequences. Prevention.
- Internal radiation dosimetry, MIRD calculations. Dose calculations – calculations of absorbed doses, therapeutic targets; tumor doses required for effective treatment.

### **Clinical requirements for radionuclide therapy**

- Qualifications of physicians: competence in: patient evaluation - to include: pertinent patient information relevant to the requested procedure using clinical request form, patient interview; chart and computer data base review; Review of relevant imaging studies. Focused physical examination as indicated; and communication with the referring physician if necessary.
- Patient care and procedural skills. History and physical exam.
- Certification in NM, NR, RO, BLS. ACLS desirable.
- Patient selection – Verification of patient identity; Explanation of procedure to the patient. Informed consent. Determination and documentation of pregnancy states. Discussion of risks and benefits of the procedure, including patient education and counseling of expected benefits, possible adverse side effects, radiation safety. Determination of clinical indication. Evaluation of findings – clinical (e.g. operative), pathology, lab values (ex. FT4, TSH, thyroglobulin, WBC, platelets), relevant imaging studies - oncologic studies, including as appropriate studies of sentinel node localization, fluorodeoxyglucose (FDG) imaging, Meta-Iodo-Benzyl-Guanidine (MIBG), somatostatin-receptor imaging, and other agents as they become available. PET, PET/CT, and other hybrid molecular imaging studies for both oncologic and non-oncologic indications.
- Patient preparation: determine desired administered activity, route of administration. Determine required dosimetry. Understand risks specific to each therapeutic radiopharmaceutical, including types of emissions.
- Patient management (along with other physicians as needed) of post-therapy complications.
- Supervision of administration of therapeutic radiopharmaceutical(s) to patient. Radiation protection specific to each therapeutic radiopharmaceutical. Dosimetry.
- Patient release – timing and conditions, provision of radiation precautions, verbal and written.
- Prepare a complete but concise nuclear medicine procedure report.
- Post-therapy follow up. Follow up scintigraphy as necessary.
- Assessment of treatment response.
- Recommend, plan, conduct, supervise, interpret, and report diagnostic and therapeutic nuclear medicine procedures appropriate for the clinical problem or condition.
- Therapeutic administration of radioiodine for both malignant and benign thyroid disease. When appropriate, thyroid studies must include measurement of iodine uptake and dosimetry calculations for radio-iodine therapy.
- Therapeutic administration of other unsealed radiopharmaceuticals for malignant and benign diseases.
- Evaluate radionuclide uptake, biodistribution, metabolism, retention and clearance with quantitative imaging to determine tumor dosimetry and therefore treatment planning.



- Understand fundamentals of imaging molecular targets, processes and events, and existing and emerging molecular imaging techniques, particularly as they relate to current clinical practice of radiopharmaceutical therapy.
- Radiopharmaceutical and/or Clinical Indications (including but not limited to):
  - o Hyperthyroidism – I-131 sodium iodide
  - o Differentiated thyroid cancer – I-131 sodium iodide
  - o Bone pain palliation – Sr-89 chloride, Sm-153 EDTMP
  - o Radioembolization for hepatocellular cancer or liver metastases – Y-90 Theraspheres or SIRSpheres
  - o Neuroendocrine tumors – I-131 MIBG, Lu-177 Dotatate and other potential PRRT therapies
  - o Radiolabeled antibodies
  - o Bone metastases - Ra-223 dichloride
  - o Prostate cancer – Lu-177 PSMA, (Ac-225 PSMA – currently under active investigation in Europe)
  - o Other therapeutic radiopharmaceuticals as they become available for clinical practice.
  - o Other potential therapeutic radionuclides currently under investigation:
    - Beta-emitters: Cu-67, Re-186, Re-188, Ho-166
    - Alpha-emitters: Bi-212, Bi-213, At-211, Tb-149, Ac-225

Please note that much of the training delineated above would be obtained within the context of nuclear medicine training programs in Nuclear Medicine or Nuclear Radiology, or training programs in Radiation Oncology. For those physicians who have not had formal training in Nuclear Medicine/Nuclear Radiology or Radiation Oncology and wish to provide radionuclide therapy, the above information is considered essential for competent practice of radionuclide therapy.

**Recommendations for initial and maintenance of competency under 35.390(b):**

- 1) Certification process for physicians performing radiopharmaceutical therapy as is already recognized under 10 CFR 35.390 (a) – ABNM or ABR NR or RO certification is sufficient.
- 2) Participation in Maintenance of Certification for those who became an authorized user through the alternate pathway, similar to 35.390(a).
- 3) Accreditation of the Nuclear Medicine laboratory. This should include a proficiency testing program that will assess performance of the technologists and physicians.

Future possible evaluation of competency under 35.390(b):

Certification of physicians who have completed a Fellowship in radiopharmaceutical therapy and have passed a certification exam by an accredited medical specialty board.



Dr. Christopher Palestro, Chairman  
Advisory Committee on the Medical Uses of Isotopes  
The U.S. Nuclear Regulatory Commission

**RE: Written Statement to the Advisory Committee on the Medical Uses of Isotopes, the Nuclear Regulatory Commission; Training & Experience Requirements**

**11 July 2018**

Dear Dr. Palestro and the Advisory Committee,

In response to the topics discussed during the Advisory Committee on the Medical Uses of Isotopes (ACMUI) meeting regarding Training & Experience (T&E) hours for AUs under 10 CFR 35.300 on March 1, 2018, Bayer HealthCare Pharmaceuticals Inc. would like to share both the real world operational safety history of Xofigo and the knowledge gained after 5 years of commercial availability to help inform the Nuclear Regulatory Commission (NRC). Bayer is requesting the NRC to consider a proposal to enable a class of physicians, notably medical oncologists and urologists, to attain Authorized User (AU) status under the limited authorization of parenteral administration of  $^{223}\text{Ra}$  dichloride (Xofigo) with 80 hours of classroom and laboratory training, as well as appropriate work experience (under the supervision of an AU for Xofigo or a Xofigo manufacturer) and written attestation. Xofigo is an FDA-approved and commercially available therapeutic agent in the United States.

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0915

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yuan.xue@bayer.com

As the NRC is aware, our distribution model limits unintended exposure and reduces the risk of misadministration since it limits the handling requirements at end user facilities to an absolute minimum.

With this demonstrably safe model of distribution along with the previously discussed reality of decreasing numbers of AUs limiting patient access to effective Xofigo treatments, Bayer is interested in identifying a path forward for other physicians to attain AU status for limited authorization to administer Xofigo to patients under their care.

**Xofigo**

Xofigo ( $^{223}\text{RaCl}_2$ ) is an alpha emitting radiopharmaceutical which is concentrated in areas of osteoblastic activity. Xofigo is currently FDA-approved for the treatment of patients with castration-resistant prostate cancer, symptomatic bone metastases and no known visceral metastatic disease. This approval was based on showing a 2.8-month survival benefit (3.6-month survival benefit at the updated analysis) over placebo during the pivotal phase III trial, ALSYMPCA (ALpharadin in SYMptomatic Prostate CAncer).

Since the launch of Xofigo in 2013 over 90,000 doses have been delivered and administered to patients at more than 1,000 sites located across the United States (Bayer internal database). During this time there have been very few cases of medication errors reported with the administration of Xofigo Patient Ready Doses in the US.

In our Phase III ALSYMPCA (ALpharadin in SYMptomatic Prostate CAncer) trial, there was a higher incidence of Grade 3/4 thrombocytopenia and neutropenia in the radium arm compared to placebo. Overall, there was a higher incidence of Grade 3 and 4 adverse events and more patients discontinuing treatment on the placebo arm than the active Ra-223 arm.

<b>Treatment-emergent AE</b>	<b>Radium (N=509)</b>	<b>Placebo (N=253)</b>
CTC Grade 3 or 4*, n (%)	339 (56)	188 (62)
Serious adverse events, n (%)	281 (47)	181 (60)
Leading to discontinuation of study treatment, n (%)	99 (16)	62 (21)

\*CTC toxicity grade: 1 = mild; 2 = moderate; 3 = severe, 4 = life-threatening; and 5 = death.

Per ALSYMPCA: “The number of patients who had adverse events after they received the study drug was consistently lower in the radium-223 group than in the placebo group for all adverse events (558 of 600 patients [93%] vs. 290 of 301 patients [96%]), grade 3 or 4 adverse events (339 patients [56%] vs. 188 patients [62%]), serious adverse events (281 patients [47%] vs. 181 patients [60%]), and study drug discontinuation because of adverse events (99 patients [16%] vs. 62 patients [21%]).”

### **US Distribution/Administration Model of Xofigo**

During the development of our distribution model for Xofigo in the United States, an unprecedented level of detail and attention was focused on ensuring that whenever possible, potential routes of exposure and contamination to end users were removed. This resulted in an operational model that provides patient-specific unit dosages in 10 mL syringes which carry both NIST traceability and a high degree of certainty that there is no external contamination.

Before the syringe containing the appropriate unit dosage of Xofigo arrives at the customer, there is an extensive amount of training and education provided by Bayer to all end users to ensure they handle and administer the unit dosage in a safe manner. Bayer has an entire team comprised of ten health physics/nuclear medicine trained individuals, called radiotherapy specialists, to assist in clinical site setup and maintenance activities as needed.

Xofigo injection does not require long infusions, pumps, or pre-meds; no significant injection site reactions have been observed with this radiopharmaceutical in the post-approval setting. An IV line is first established with saline to ensure patency, then the Xofigo-containing unit dosage syringe is connected via a three way stopcock (or similar) followed by a slow bolus injection over one minute. After another saline flush, all potentially contaminated materials are segregated and bagged for decay-in-storage. Due to the decay characteristics of the alpha-emitting radiopharmaceutical, external exposure is not an operational concern and internal contamination is effectively managed by using standard universal precautions. The patient is also immediately releaseable without instructions per 10 CFR 35.75(b). The dose associated with a Xofigo patient (1.6 mrem per NUREG-1556) to members of the public is less than 2% of the NRC limit for which instructions are required; for scale this is roughly the equivalent to the radiation dose experienced on a two hour plane flight. This treatment process is then repeated up to 5 more times separated in time by 4 weeks (8 weeks maximum).

### **NRC AU Licensing of Xofigo**

In the fall of 2012, Bayer Healthcare along with the product inventor Algeta were asked to provide some background to the NRC on the health physics considerations of Xofigo usage, a first in class drug, to help inform the licensing decision. Subsequently in January 2013, the NRC announced that Xofigo would be licensed under 10 CFR 35.300, with T&E requirements pursuant to either 10 CFR 35.390 or 35.396, allowing nuclear medicine physicians/radiologists and radiation oncologists to be AUs for the administration of Xofigo (an alternate pathway involving the completion of 700 hours of T&E was available for any other physician to attain such AU status).

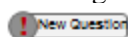
## Issues with the current T&E requirements

While this model has worked well in the past, issues have now surfaced that limit patient access, despite the fact that these patients are indicated and eligible for Xofigo treatment. Some of the most prevalent issues are:

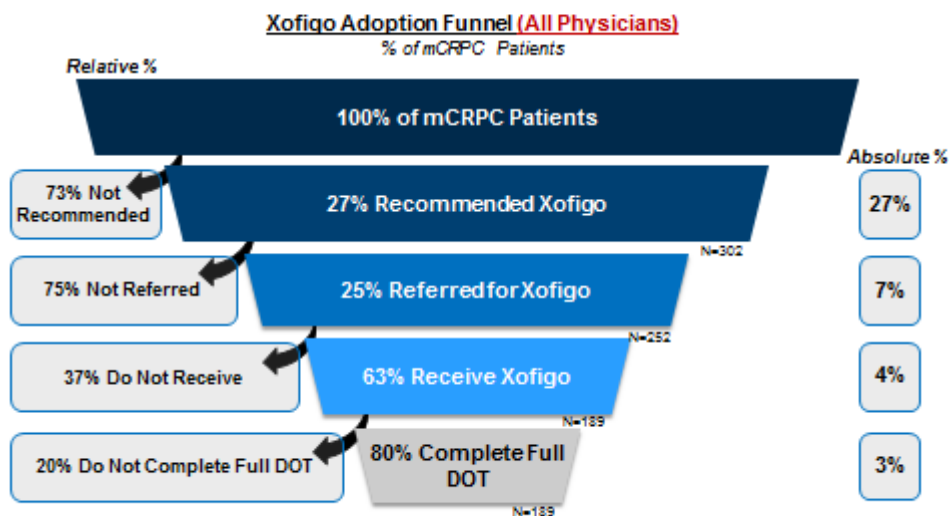
- Diminishing numbers of AUs
- Geographic distribution of Authorized Users
- Extraordinary interest within the referring physicians community to administer Xofigo themselves allowing for simplification and optimization of patient experience.
  - These physicians are also in many cases the most appropriately aligned with the clinical and safety benefits of Xofigo and the continuum of patient care.
- Logistical and financial burdens for patients being forced to visit different offices at different times during the course of treatment
- The referring physicians, instead of the administering physicians, historically manages the treatment of adverse events related to Xofigo and other systemic therapies

These considerations and hurdles do limit the access of patients to Xofigo as discussed immediately below (additional information can be provided as needed). Xofigo is a product which carries a NCCN Category I recommendation.

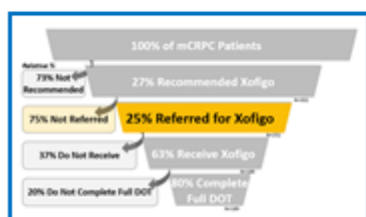
Below are diagrams illustrating this access limitation:



Physicians do not refer 75% of patients for Xofigo despite making a recommendation



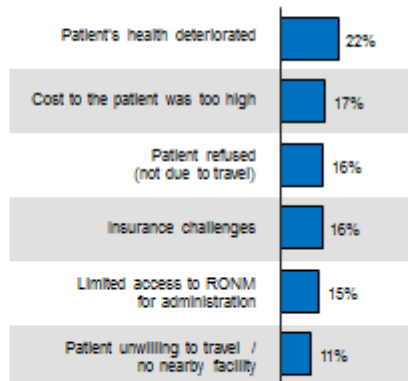
Patient health deterioration is a key reason for loss of referral



**75%**

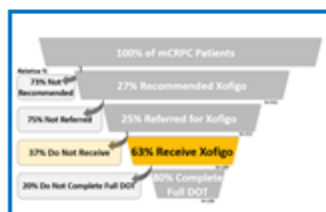
of mCRPC patients *recommended* for Xofigo are *NOT* referred for Xofigo (among All Physicians)

#### Reasons for Not Referring Patients for Xofigo Despite Recommendation (Aided)



N=273  
All MDs

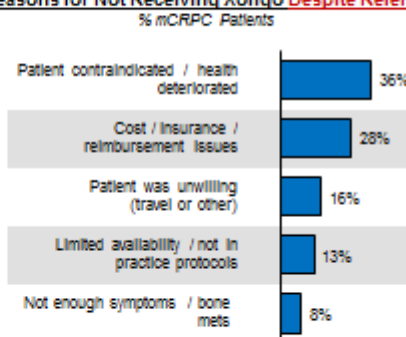
When Xofigo is not received despite a referral, this is most often because of lack of eligibility or cost/ reimbursement issues



**37%**

of mCRPC patients *referred* for Xofigo do *NOT* receive Xofigo (among All Physicians)

#### Reasons for Not Receiving Xofigo Despite Referral



N=136  
All MDs

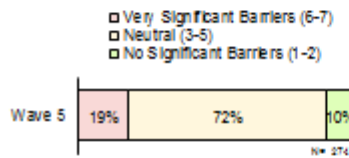
These diagrams indicate that of the 27% of patients who physicians recommend for Xofigo, only 25% are referred to a neighboring clinic for treatment. Even after a referral, 37% of patients don't end up getting Xofigo.

In addition, this patient-access limitation was also confirmed in additional market research:

20% of physicians indicate availability of a Nuc Med specialist/facility as a top 3 barrier to prescribing Xofigo

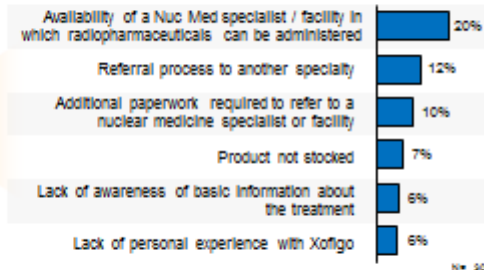
#### Physicians with Significant Barriers for Xofigo

% Uros & Oncs rating 6-7 on 7-pt scale where 1 is "No Significant Barriers" and 7 is "Very Significant Barriers"



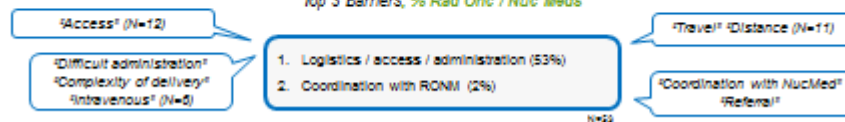
#### Referral Barriers to Xofigo Prescribing and Administration (Aided)

% Uros & Oncs selecting among the top 3 barriers



#### Referral Barriers for Xofigo (Unaided)

Top 3 Barriers, % Rad Onc / Nuc Meds



Page 1

## Proposed path forward

These issues were discussed during the March 1, 2018 ACMUI meeting. It is recognized that an environment is being created in which not all the patients prescribed Xofigo treatment during the course of their disease are actually getting it.

Of importance to the regulatory scope of the NRC are the unique radiation safety considerations that make Xofigo a safe and easy to use product based both on emission characteristics, ease of administration and minimal administered activity. A considerable investment was made to ensure the product is both received and eventually dispensed in a fashion where operational risk is mitigated by engineering controls and in those areas where this is not possible, appropriate expert training is provided by Bayer.

Therefore, Bayer respectfully requests that the NRC allows for the licensers of physicians *vis a vis* T&E under the current distribution model after the completion of training/experience/competency requirements provided by the manufacturer OR other appropriately-trained Authorized Users.

If there are any questions regarding this statement, please contact me at yuan.xue@bayer.com or at 862-404-4057.

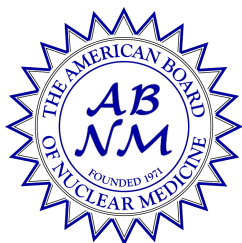
Respectfully yours,

Yuan Xue, PhD  
Global Regulatory Strategist  
Regulatory Affairs – Oncology  
Bayer HealthCare Pharmaceuticals

## References:

1. Xofigo US Packaging Insert.

2. Bayer internal database.
3. Bayer Responses to NRC Questions: Radium-223 dichloride; dated 8-November-2012.



# The American Board of Nuclear Medicine

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July 31, 2018

Christopher Palestro, M.D.

Chair, Advisory Committee on the Medical Uses of Isotopes  
U.S. Nuclear Regulatory Commission  
Washington, DC 20555-0001

Dear Dr. Palestro:

The ABNM has reviewed the February 19, 2018 draft report of the ACMUI Subcommittee on Training and Experience Requirements for All Modalities regarding the current NRC requirements for 700 hours of supervised training and experience for Authorized Users (AUs) of radioactive materials under 10 CFR 35.390 – Training for use of unsealed byproduct material for which a written directive is required. The Subcommittee is considering whether the 700 hour training requirement decreases patient access to alpha and beta emitting therapeutic radiopharmaceuticals, and whether it should recommend changes for the total number of hours of training & experience that is required.

The Subcommittee draft interim report states there are two reasons for reasonable concern for a near-future decline in patient access to care: (1) U.S. Food and Drug Administration's approval of  $^{177}\text{Lu}$  dotatate for treatment of certain neuroendocrine tumors, and (2) the decrease in the number of first-time candidates sitting for the Certification Examination of the American Board of Nuclear Medicine.

The ABNM welcomes the FDA-approval mentioned above and supports efforts to bring more targeted radionuclide therapies to patients in the U.S.; however, the ABNM strongly believes that the current requirement for 700 hours of supervised training and experience should not be changed and that reducing the *minimum* requirement for 700 hours of supervised training and experience for unsealed radioisotope therapy raises concern for patient safety. The decrease in the number of nuclear medicine or nuclear radiology qualified AUs is likely overestimated in the Subcommittee draft interim report. The need for fact-driven evaluation before any action was also endorsed by the American College of Radiology (ACR) in comments to the NRC ACMUI sent on July 16. The ABNM fully supports the ACR statement.

The number of initial ABNM certificates issued each year has been relatively constant from 1977 – 2015. The average number of certificates issued each year was 72 during this time (range 50 – 107). The ABNM issued 43 initial certificates in 2016, and 49 certificates in 2017. No data is available for 2018 since the certification examination will not be given until October.



The ABNM has issued a total of 5,744 certificates since the board was incorporated in 1971. There are at least 3,591 active diplomates (not deceased or retired) at the present time.

The Subcommittee draft interim report noted a decrease in the number of ACGME accredited Nuclear Medicine training programs and residents from 57 programs with 161 residents in academic year 2007 – 2008, to 41 programs with 75 residents in 2017 – 2018.

The decrease in the number of programs and trainees is partly due to an increase in the number of Nuclear Medicine physicians who are also certified in Diagnostic Radiology by the American Board of Radiology (ABR). Certification by the ABR decreases the duration of Nuclear Medicine training required for ABNM certification from 36 months to 16 months, creating the appearance of decreasing numbers of residents, when it is the duration of training that is decreasing. Contributing to this trend is the increasing availability of dual training pathways where residents training in Nuclear Medicine are counted as Diagnostic Radiology residents rather than Nuclear Medicine residents, due to the requirements of the ACGME and the ABR. At a recent professional meeting, the ABNM learned that there are at least 35 additional radiology residents engaged in a new program through the ABR aimed at additional qualification in nuclear radiology during the usual length of their diagnostic radiology residency.

The ABNM believes that dual training will result in better-trained physicians to meet the needs of patients in the era of molecular imaging and therapy. The ABNM sees no evidence that workforce issues have decreased patient access to care, and concern for potential future issues has not considered recent positive changes in Nuclear Medicine training. The popularity of the dual training pathways in Nuclear Medicine and Diagnostic Radiology is one of the reasons for the decline in the number of ACGME accredited Nuclear Medicine programs; however total number of residents is not reflected in a similar decline in number of ABNM certificates.

The ABNM urges the subcommittee to re-evaluate the initial estimates of AUs available and those in training to provide the needed services. We also request a re-review of the number of radiation oncology physicians in training as numbers quoted in the draft interim report were erroneously low.

In addition, targeted radionuclide therapies frequently require management by experts in multiple disciplines (surgery, radiation oncology, medical oncology, radiology, nuclear medicine) at centers of excellence; no shortage of AUs has been reported at such institutions. Finally, if the current number of AUs proves to be insufficient to make radionuclides widely available, we believe pursuing approaches to increase the number of properly trained nuclear medicine physicians, nuclear radiologists and radiation oncologists will be better for patient care than lowering the standards for administering radionuclide therapies.

Although the NRC does not oversee the insurance industry, we feel that a larger threat to patient access as compared to the number of AUs in the United States is insurance coverage.

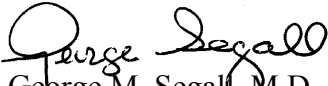
Reducing the *minimum* requirement for 700 hours of supervised training and experience for unsealed radioisotope therapy further jeopardizes patient safety because there is no standardized


***ABNM Letter to ACMUI on Training and Experience***

assessment of the knowledge, skill and judgment of these physicians who are not certified by the ABNM, or certified by the ABR in the subspecialty of Nuclear Radiology.

In summary, the ABNM strongly believes that the current requirement for 700 hours of supervised training and experience should not be changed and asks the NRC correct the errors in the number of trainees, which we would expect could reduce or end the concern on the number of AUs available to provide these services.

Sincerely,

  
George M. Segall, M.D.  
Executive Director

  
Daniel A. Pryma, MD  
Chair

GMS/DAP/mrf



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August 22, 2018

Christopher Palestro, MD

Chair, Advisory Committee on the Medical Uses of Isotopes

US Nuclear Regulatory Commission

Washington, DC 20555-0001

Dear Dr Palestro,

The leadership of the ABR reviewed the February 19, 2018 and July 5, 2018 draft reports of the ACMUI Subcommittee on Training and Experience Requirements for All Modalities regarding the current NRC requirements of 700 hours of supervised training and experience for Authorized Users (AUs) of radioactive materials under 10 CFR 35.390, *Training for use of unsealed byproduct material for which a written directive is required*. The subcommittee has suggested that the 700-hour training requirement might be reduced, partly because of a perceived decrease in patient access to care with alpha and beta emitting therapeutic radiopharmaceuticals.

The ABR board strongly opposes a reduction in the current training requirements or development of a "limited status AU". This is a patient safety and quality-of-care issue. As this field becomes more complex, it is important to maintain strong training requirements.

The subcommittee mentions shortages in the number of AUs in the United States. We are not aware of any shortage. The ABR and ABNM have not seen decreases in the number of candidates seeking certification in nuclear medicine or nuclear radiology (nuclear radiology is the term used by the ABR for our candidates and diplomates, whereas nuclear medicine is usually practiced by non-ABR certified individuals who are certified only by ABNM). It is true that there has been a decline in the number of "Nuclear Medicine Residency Programs", largely because of the increasingly limited job market for individuals without strong diagnostic radiology (DR) training in this era of hybrid imaging (PET/CT, SPECT/CT, PET/MR), which requires substantial knowledge of all aspects of DR modalities. However, in DR, there has been increased interest in nuclear radiology *because* of hybrid imaging and new therapeutic radioisotopes. DR residency programs are *not* closing and there are increased opportunities for nuclear radiology training in DR programs. The number of radiation oncology (RO) residents and candidates for ABR RO certification has been stable for many years. Most ABR DR and RO diplomates are AU Eligible at the time of certification, and most go on to become AUs.

In summary, the ABR strongly opposes a reduction in the number of hours of supervised training and experience for AUs under 10 CFR 35.390. We feel that maintenance of the current 700 hours is necessary to protect the public.

Sincerely,

Lisa A Kachnic, MD  
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Valerie P. Jackson, MD, Executive Director

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**QUALITY IS OUR IMAGE**

August 27, 2018

Attn: The Honorable Kristine L. Svinicki  
U.S. Nuclear Regulatory Commission  
Mail Stop O-16B33  
Washington, DC 20555-0001

**Subject: 10 CFR 35.390, "Training for use of unsealed byproduct material for which a written directive is required;" recommendations of the American College of Radiology**

Dear NRC Chairman Kristine Svinicki:

On behalf of the American College of Radiology (ACR)—a professional organization representing more than 38,000 radiologists, radiation oncologists, interventional radiologists, nuclear medicine physicians, and medical physicists—we are writing regarding ongoing activities within the U.S. Nuclear Regulatory Commission (NRC) and the NRC Advisory Committee on the Medical Uses of Isotopes (ACMUI) to reevaluate authorized user (AU) requirements in 10 CFR Part 35, Subpart E—particularly 35.390, *"Training for use of unsealed byproduct material for which a written directive is required."* This letter outlines specific concerns of ACR on this topic, and proposes an alternative approach going forward.

**Concerns Regarding NRC Activities Related to 10 CFR 35.390**

The ACR supports and acknowledges the appropriateness of periodic reassessment of 10 CFR Part 35 to provide reasonable assurance of adequate protection of public health and safety. We believe that this process should be driven by the experiences and expertise of medical licensees and regulators, informed by objective and quantitative evidence, and be free from politicization by external companies and groups. We are concerned that the current efforts to reevaluate the training and experience (T&E) requirements in 10 CFR 35.390 appear to have been hastened by external pressures without a sufficient basis in science or the shared experience of current materials licensees. Recent NRC activities to prioritize and rapidly move toward modifying the T&E requirements in 10 CFR 35.390 for prospective AUs without NRC-recognized board certification deviate from the data-driven, risk-informed, deliberative approach warranted by the associated risk and potential destabilizing impact of such a policy.

The ACR believes the arguments in favor of significantly modifying 10 CFR 35.390 to provide a less comprehensive alternate pathway for those without NRC-recognized board certification are

unsubstantiated and should be examined with scientific rigor before the NRC takes any significant action that could negatively impact public health and safety. The recent NRC staff efforts at the Commission's direction to reimagine a radionuclide-specific, "limited scope AU" concept for uses under 10 CFR Part 35, Subpart E do not adequately address the primary questions of whether regulatory revisions are a necessary and justifiable use of limited NRC resources, and whether the perceived benefits outweigh the substantial risks.

### **A Multidisciplinary Team Model is the Standard of Care in Radiopharmaceutical Therapy**

As part of a broad spectrum of cancer therapy modalities, therapy with unsealed radiopharmaceutical sources may promote cures or palliation of disease while minimizing untoward side effects and complications.<sup>1</sup> Examples of these radiopharmaceuticals include Iodine-131 (sodium iodide), Iodine-131 (meta-iodobenzylguanidine MIBG iodine-131), Lutetium-177 DOTA, Yttrium-90 DOTA, Phosphorus-32 (sodium phosphate), Phosphorus-32 (colloidal chromic phosphate), Radium-223 (radium dichloride), Samarium-153 (lexidronam ethylene diamine tetra methylene phosphonic acid [EDTMPA]), Strontium-89 (strontium chloride), Yttrium-90 (ibritumomab tiuxetan), and others in current research.

The predominant medical paradigm for treating patients who may require such therapy utilizes a multidisciplinary team approach so patients benefit from the unique expertise of many medical specialties. Within that framework, public health and safety are optimally protected when unsealed radiopharmaceutical therapies are supervised and performed by appropriately trained and licensed physicians. Typically these are nuclear medicine physicians, radiation oncologists, nuclear radiologists, and certain other diagnostic radiologists with those qualifications in close cooperation and communication with referring physicians responsible for overall clinical management of the patients (such as medical oncologists, etc.), and supported by staff trained and experienced in handling of radioactive materials and imbued with a culture of safety for patients and personnel.<sup>2</sup>

### **Lack of Data Indicating AU Shortage**

NRC's exploration of less comprehensive, radionuclide-specific, "limited scope" pathways to AU status for therapeutic radiopharmaceuticals implies that the agency believes there is an insufficient AU population performing and supervising radiopharmaceutical therapies in the United States. This presumption has not been supported by publicly accessible, trustworthy data compiled by first-party sources. Indeed, no such datasets currently exist despite questions about the size and distribution of AUs for specific medical uses of isotopes.

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<sup>1</sup> ACR, American Association of Physicists in Medicine (AAPM), and Society for Pediatric Radiology (SPR). *ACR-AAPM-SPR Technical Standard for Therapeutic Procedures Using Radiopharmaceuticals*. Available from <https://www.acr.org/-/media/ACR/Files/Practice-Parameters/RadioPharm.pdf>

<sup>2</sup> American College of Radiology (ACR). *ACR Practice Parameter for the Performance of Therapy with Unsealed Radiopharmaceutical Sources*. Available from: <https://www.acr.org/-/media/ACR/Files/Practice-Parameters/UnsealedSources.pdf?la=en>

In March 2018, an NRC ACMUI subcommittee discussed a potential future AU shortage based on nuclear medicine residency trends combined with an expectation of Lu-177 dotatate popularity. However, those preliminary discussions focused exclusively on previous American Board of Nuclear Medicine (ABNM) trends, without factoring in the American Board of Radiology (ABR) radiation oncology and nuclear radiology pathways to AU status for unsealed radiopharmaceutical sources requiring a written directive. Our current understanding, based on information from the ABR, indicates a potentially increasing trend in the radiation oncologist population and increased expansion of recently revamped nuclear radiology programs. The ACMUI's July 5, 2018 comments to NRC staff found that nearly 900 residents in radiation oncology, nuclear medicine, nuclear radiology, and the redesigned radiology pathway could potentially meet the AU T&E requirements in 10 CFR 35.390 for the 2017-2018 academic year.<sup>3</sup> Thus, residency information and observations from the specialties in question contradict the unsubstantiated premise of an impending AU shortage. The increasing clinical use of Lu-177 dotatate, and theranostics in general, should continue to bolster medical student interest in pursuing specialty residencies with radiopharmaceutical therapy expertise. However, there is a need for trustworthy data about currently active AU populations.

The ACR recommends that NRC collaborate with Agreement States and broad-scope licensees to determine the number and distribution of actively practicing AUs with the therapeutic radiopharmaceuticals of interest. Maintaining this dataset should illustrate AU trends over a multi-year period to deduce the stability and growth of the AU population. Changes in AU numbers over time could provide regulators and stakeholders with informed arguments supporting or opposing regulatory revisions and would serve as an accurate baseline for future decision-making.

#### **Other Factors Driving Utilization of Radiopharmaceutical Therapy Unrelated to NRC Regulations**

NRC's hastened progression towards a radionuclide-specific, limited scope AU pathway also implies that radiopharmaceutical therapies are underutilized perhaps because of the presumption that AUs are insufficiently accessible under the current T&E prerequisites in 10 CFR 35.390. While there is certainly no trustworthy evidence to suggest chronic underutilization of these modalities resulting from current NRC regulations, there are myriad drivers behind care management decisions by referring clinicians.

While practice guidelines, clinical decision support tools, peer-reviewed literature, and other informational resources can augment decision-making, medical oncologists and other referring physicians responsible for managing patients' care have varying levels of awareness regarding the availability and appropriate use of radiopharmaceutical therapy options. In many cases, alternative treatments not involving radiation dose are available with similar appropriateness ratings and outcomes. In some cases, there could be reluctance by care managers to refer/transfer patients for subspecialty care regardless of the proximity, expertise, or quality of care performed by providers of

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<sup>3</sup> NRC ACMUI. *Advisory Committee on the Medical Uses of Isotopes Comments on the Draft SECY Paper Entitled "Staff Evaluation of Training and Experience Requirements for Administering Radiopharmaceuticals."* Available from: <https://www.nrc.gov/docs/ML1818/ML18186A517.pdf>



cancer therapies outside their own practices. Economic/insurance drivers and patients' personal views about radiation could also affect referral and treatment decisions. The ACR recommends further exploration of utilization drivers that include partnerships with other federal regulatory agencies with more influence than NRC on radiopharmaceutical therapy utilization, such as the Centers for Medicare and Medicaid Services (CMS).

It is unclear what effects, if any, future modifications to NRC T&E requirements for prospective AUs without NRC-recognized board certification would have on referral patterns and overall use of radiopharmaceutical therapies. NRC regulations are not the sole external consideration for providers interested in providing radiopharmaceutical therapy themselves. A myriad of factors – such as medical standards, appropriate use criteria, practice/procedure guidelines, facility accreditation requirements, quality metrics, insurance/payer requirements, self-referral prohibitions, medicolegal considerations, etc. – influence physician and provider willingness to offer any given treatment. Regardless, if NRC moves forward with the requested revisions to 10 CFR 35.390, it is likely that referring clinicians without subspecialized expertise would be pressured for financial reasons by manufacturers to obtain “limited scope AU” status—those same outreach efforts by manufacturers might be better used to educate the referring provider community about the availability of these therapies provided by subspecialized experts.

#### **Therapeutic Radiopharmaceuticals are Not Simple and Safe—Need for Specialized Expertise**

Patients and their families expect that those performing and supervising radiopharmaceutical therapy are providing the right treatment at the right dose at the right time. Nuclear medicine physicians, radiation oncologists, and nuclear radiologists are continuously immersed in radiological considerations as an inherent component of their subspecialized roles on the patient's care team. Such considerations are integrated into every level of training programs, certifications, specialty publications, and day-to-day professional responsibilities. Outliers from other medical specialties who have obtained the necessary T&E and supervised cases under the current 10 CFR 35.390 have acquired basic knowledge to competently manage these tasks in a responsible manner—this is why 10 CFR 35.390 already includes a legitimate T&E alternative pathway to AU status for those from other specialties without NRC-recognized board certification.

With any radionuclide-specific, “limited scope AU” concept, NRC should consider the much higher likelihood of safety issues when enabling the use of therapeutic radiopharmaceuticals in settings with limited expertise and experience in nuclear materials handling, storage, shipping, dosimetry, and waste handling. AUs must be fully prepared to supervise all aspects of the medical use of the unsealed radiopharmaceutical sources in question, prevent potential medical events before they occur, identify and report to regulatory agencies any medical events that have occurred, and mitigate any dangers of spills and contamination.

#### **Prepackaged Unit Dose Distribution Does Not Eliminate Need for Expertise**

The core knowledge required to adequately perform AU responsibilities remains the same regardless of whether radiopharmaceuticals are shipped from centralized nuclear pharmacies in unit doses or

prepared on-site in the treatment facilities. Many issues and risks—i.e., improper assay, spillage/contamination, handling unused product, tissue extravasation, etc.—would be more likely to occur in settings where the AU is nominally trained and generally unaccustomed to working with unsealed radiopharmaceutical sources. Less than perfect real-world scenarios, including unexpected situations during the handling of these materials, must be factored into the NRC’s regulatory approach.

#### **Alpha- and Beta-Emitters**

NRC should not assume that specific uses regulated under 10 CFR Part 35, Subpart E are safe for general use if they involve alpha- and/or beta-emitters. Many such agents will have a gamma component or be paired with gamma-emitting agents to allow for imaging that is essential for whole body and organ dosimetry and therapeutic decision-making. It is inaccurate to suggest that these radiopharmaceuticals can be handled by nominally trained clinicians in inexperienced facilities without introducing risk to all involved.

#### **Chemotherapy Drugs Are Not Radioactive**

It has been argued that medical oncology practices are experienced with administration by oncology nurses of hazardous drugs, such as antineoplastic agents used in chemotherapy. However, nuclear materials pose very different dosage, exposure, handling, storage, waste management, and risk mitigation considerations compared to nonradioactive hazardous materials. While antineoplastic agents are certainly harmful in terms of occupational exposure for oncology nurses when absorbed into the skin/inhaled/ingested, such agents do not carry the same exposure and environmental concerns—much less the same level of public fear and panic—as nuclear materials generally do.

To be clear, the fact that referring physicians may supervise treatments that involve pharmacist preparation and oncology nurse administration of antineoplastic agents or other hazardous drugs in no way prepares them for their responsibilities as an AU of radiopharmaceuticals to protect patients, their staff and facilities, and members of the public from ineffective, accidental, inappropriate, or otherwise unnecessary radiation exposure.

#### **Unintended Implementation Consequences and Considerations for NRC and Agreement State Regulators of Radionuclide-Specific, Limited Scope AU Concept**

Beyond the more important medical and public health/safety considerations, the ACR has concerns about the likely disruption within NRC, state regulatory agencies, and licensed facilities created by establishing and overseeing additional complexity and disparate AU levels with varying responsibilities (e.g., “full scope” and “limited scope/radionuclide-specific” AUs).

NRC and Agreement State agencies would need to dedicate additional resources to deal with regulatory revisions and corrections, guidance revisions and new information notices targeted to non-expert AU subpopulations, outreach to new medical communities unaccustomed to NRC’s regulatory paradigm, expanded capabilities for when spills and other adverse issues arise in nontraditional care settings, and so on. With a radionuclide-specific approach, NRC would need to establish a highly prioritized and expeditious timeframe for rulemakings intended to incorporate new radiopharmaceuticals into the



armamentarium of medical licensees and to prevent future delays in patient access to emerging agents tied to the agency's administrative processes. It would be advisable for NRC to establish a more extensive monitoring program to specifically track medical events, trends, and determine any underreporting of medical events that occur under the supervision of limited scope AUs separately from medical events that occur in the more traditional care settings. Additionally, NRC would increase its own exposure to U.S. Government Accountability Office and other external investigations of the agency's licensee vetting processes as numerous new individuals from previously unknown medical settings would be encouraged by manufacturers to seek limited scope AU status. All of the above expanded capabilities would inevitably result in increased fees for materials licensees, and less efficient/timely regulatory oversight.

#### **Summary of ACR Recommendations**

In conclusion, the ACR recommends that NRC not pursue regulatory revisions to accommodate the concept of a radionuclide-specific, limited-scope AU status until such time as NRC's time-tested paradigm in 10 CFR 35.390 is shown by data to be problematic for medical licensees or otherwise in immediate need of revision. We recommend that NRC collaborate with all Agreement State agencies and NRC broad-scope licensees to compile a multi-year dataset on the active AU population. NRC should also work with other federal agencies, particularly CMS, to explore other possible radiopharmaceutical therapy drivers and determine if NRC's AU T&E requirements in 10 CFR 35.390 are directly causing a perceived underutilization. Most importantly, we recommend that NRC consider the numerous unintended consequences and likely negative effects on public health and safety, security, and practice of medicine of revising 10 CFR 35.390 to provide a radionuclide-specific, limited-scope AU pathway for nominally trained clinicians.

As always, the American College of Radiology welcomes additional dialog with the NRC Commissioners and staff on these and other issues of shared interest. Please contact Gloria Romanelli, JD, ACR Senior Director, Legislative and Regulatory Relations, or Michael Peters, ACR Director of Legislative and Regulatory Affairs, at (202) 223-1670 or [gromanelli@acr.org](mailto:gromanelli@acr.org) / [mpeters@acr.org](mailto:mpeters@acr.org), with any questions or concerns.

Respectfully Submitted,



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