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NUCLEAR REGULATORY COMMISSION

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ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

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TUESDAY,

SEPTEMBER 10, 2019

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The meeting was convened in room T2D30 of Two White Flint North, 11555 Rockville Pike, Rockville, Maryland, at 8:30 a.m., Christopher J. Palestro, M.D., ACMUI Chairman, presiding.

MEMBERS PRESENT:

CHRISTOPHER J. PALESTRO, M.D., Chairman

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

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

A. ROBERT SCHLEIPMAN, Ph.D., Member

MICHAEL SHEETZ, Member

MEGAN L. SHOBER, Member

HARVEY WOLKOV, M.D., Member

NRC STAFF PRESENT:

KRISTINE SVINICKI, Chairman of the U.S. Nuclear Regulatory Commission

JOHN LUBINSKI, Director, Office of Nuclear Material Safety and Safeguards (NMSS)

ROB LEWIS, Deputy Director, NMSS

ANDREA KOCK, Director, Division of Material Safety, State, and Tribal Programs

CHRIS EINBERG, DFO, NMSS/MSEB

MARYANN AYOADE, NMSS/MSEB

LISA DIMMICK, Team Lead, NMSS/MSEB

TOMAS HERRERA, NMSS/MSST

VINCE HOLAHAN, PhD, NMSS/MSST

DONNA-BETH HOWE, PhD, NMSS/MSEB

IAN IRVIN, OGC

KELLEE JAMERSON, ACMUI Coordinator, NMSS/MSEB

SARAH LOPAS, NMSS/MSEB

TIM MOSSMAN, NMSS/SMPB

KATIE TAPP, PhD, NMSS/MSEB

IRENE WU, NMSS/MSEB

MEMBERS OF THE PUBLIC PRESENT:

ASHLEY COCKERHAM, Mercurie Consulting

LELAND COGLIANI, *Unaffiliated*

MIGUEL de la GUARDIA, *Unaffiliated*

MATT DENNIS, CRD Associates/Lucerno Dynamics

CAITLIN KUBLER, Society of Nuclear Medicine and Molecular Imaging

RONALD LATTANZE, Lucerno Dynamics

CAROL MARCUS, *Unaffiliated*

RICHARD MARTIN, American Association of Physicists in Medicine

MICHAEL PETERS, American College of Radiology

JOE RUBIN, *Unaffiliated*

NAN SILVERMAN-WISE, National Nuclear Security Administration (NNSA)

MALIKA TAALBI, NNSA

CONTENTS

P R O C E E D I N G S

8:40 a.m.

MR. EINBERG: Good morning, everybody.

I'm going to open the meeting with the Designated Federal Official opening remarks.

We're waiting on a couple of people. We're waiting on one person, but we'll go ahead and get started.

Dr. Wolkov is going through badging right now. And so, we're doing most of the administrative things right now, and hopefully, he will be back for the better part of the meeting.

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

My name is Chris Einberg. I am the Branch Chief of the Medical Safety and Events Assessment Branch, and I've been designed as the federal officer for this Advisory Committee, in accordance with 10 CFR Part 7.11.

Present today as the Designated Federal Officer and ACMUI Coordinator is Kellee Jamerson.

This is an announced meeting of the Committee and is being held in accordance with the rules

and regulations of the Federal Advisory Committee Act and the Nuclear Regulatory Commission.

This meeting is being transcribed by the NRC, and it may also be transcribed or recorded by others.

The meeting was announced in the August 13, 2019 edition of The Federal Register, Volume 84, page 401-06.

The function of the Committee is to advise the staff on issues and questions that arise on the medical use of byproduct material. The Committee provides counsel to the staff but does not determine or direct the actual decisions of the staff or the Commission. The NRC solicits the views of the Committee and values their opinions.

I request that, whenever possible, we try to reach a consensus on the various issues that we will discuss today, but I also recognize that there may be a minority or dissenting opinion. If you have such opinions, please allow them to be read into the record.

At this point, I would like to perform a roll call of the ACMUI members participating today.

Dr. Christopher Palestro, Chairman, Nuclear Medicine Physician?

CHAIRMAN PALESTRO: Present.

MR. EINBERG: Dr. Darlene Metter, Vice Chairman, Diagnostic Radiologist?

VICE CHAIR METTER: Present.

MR. EINBERG: Dr. Vasken Dilsizian, Nuclear Cardiologist, has another engagement. So, he's not here.

Dr. Ronald Ennis, Radiation Oncologist?

MEMBER ENNIS: Here.

MR. EINBERG: Mr. Richard Green, Nuclear Pharmacist?

MEMBER GREEN: Present.

MR. EINBERG: Ms. Melissa Martin also has another engagement -- Nuclear Medicine Physicist -- and will not be here.

Dr. Michael O'Hara, FDA representative?

MEMBER O'HARA: Here.

MR. EINBERG: Dr. Zoubir Ouhib, Radiation Therapy Physicist?

MEMBER OUHIB: Here.

MR. EINBERG: Dr. A. Robert Schleipman, Health Care Administrator?

MEMBER SCHLEIPMAN: Here.

MR. EINBERG: Mr. Michael Sheetz, Radiation Safety Officer?

MEMBER SHEETZ: Present.

MR. EINBERG: Ms. Megan Shober, State Government Representative?

MEMBER SHOBER: Present.

MR. EINBERG: Dr. Harvey Wolkov, as I mentioned, has to go through badging. And he's a Radiation Oncologist, and he will be joining us shortly.

There is a quorum here. So, we have at least six members.

At the table we also have Dr. Hossein Jadvar and Mr. Gary Bloom, who are new members to the Committee. And so, we welcome them. Dr. Jadvar has been selected as the ACMUI Nuclear Medicine Physician representative, and Mr. Bloom has been selected as the ACMUI Patient Rights Advocate representative. Both are pending security clearance but may participate in the meeting. However, they currently do not have voting rights. But we encourage their participation.

All members of the ACMUI are subject to federal ethics laws and regulations and receive annual training on these requirements. If a member believes that he or she may have a conflict of interest, as that term is broadly used within 5 CFR Part 2635, with regard to an agenda item to be addressed by the ACMUI, this member should divulge it to the Chair and the Designated Federal Officer, that being myself or Kellee, as soon

as possible before the ACMUI discusses it as an agenda item.

ACMUI members must recuse themselves from participating in any agenda item in which they may have a conflict of interest unless they receive a waiver or prior authorization from the appropriate NRC official.

I would like to add that this meeting is being broadcast via the NRC webcast portal. So, other individuals may be watching online. We have a virtual line available, and that phone number is 888-396-8716, once again, 888-396-8716. The passcode to access the bridgeline is 82477#, 82477#.

The handouts and the agenda items for this meeting are available on the NRC's ACMUI public website.

Individuals who would like to ask or make comments regarding a specific issue that the Committee has discussed should request permission to be recognized by the ACMUI Chairman, Dr. Christopher Palestro. Dr. Palestro, at his option, may entertain comments or questions from members of the public who are participating with us today. Comments and questions are usually addressed by the Committee near the end of the presentation and after the Committee has fully discussed the topic.

We ask that one person speak at a time, as this meeting is also closed captioned.

At this time, I ask everyone on the call who is not speaking to place their phones on mute. If you do not have the capability to mute your phone, please press *6 to utilize the conference line mute and unmute functions.

At this point, I would like to turn the meeting over to Ms. Andrea Kock, who is the Director of the Division of Materials Safety, Security, State, and Tribal Programs, for some opening remarks.

MS. KOCK: Good morning.

Can you all hear me? Good.

Welcome to the fall ACMUI meeting. I appreciate all of your time to travel here and be with us today over the next couple of days for what looks like a packed agenda.

I just wanted to welcome all the Committee members as well as members of the public who have come today to listen-in and participate in the discussion. I appreciate that everybody has very busy schedules and commitments, and it's important to us that you've made the time to be here.

I am the Director of the Division of Materials Safety, Security, State, and Tribal Programs.

I look forward to the discussions with you. I think I've met some of you over the years. I've been in about 12 different positions at the Agency that have had varying levels of interactions with the ACMUI over the years. So, I've probably met some of you here and there, and others I haven't. So, I'm looking forward to meeting those of you that I have not met.

I just also wanted to take a minute to thank the ACMUI for all of your hard work. As much as I've been involved with medical issues at the NRC for years, it was still striking to me when I came to this Division the number of issues that the ACMUI is dealing with and the thoroughness of your work. We appreciate that. Medical issues are very complex, have different facets to them. And so, your opinion is very important to us.

I also appreciate the Committee's responsiveness to issues that have come up. Sometimes in the process of business we have issues that are more emergent and we're looking for your quick feedback, and you all have been very responsive to be able to provide that to us. And we really appreciate that.

So, I just wanted to highlight a few things that we're going to talk about over the next couple of days. There's one issue that is what we call

Commission-related activity or an issue that we will bring to our Commission in the next few months. And that's the issue of training and experience requirements. You're all probably familiar that we have had a series of public meetings this past spring on this issue to look at proposals for limited scope Authorized Users. This activity was directed by our Commission. And so, we'll be writing an options paper to our Commission later on this year, based on your feedback and the feedback from our other stakeholders. So, I'm looking forward to that discussion today.

And just as I mentioned, T&E, like many other medical issues, is very complex. There's no shortage of opinions on where we should go on that. And it also has large implications for the medical and regulatory community. So, we're really looking forward to your input on that.

I just wanted to recap a couple of ACMUI meetings that have happened since the spring meeting. You all have been very, very active. Back in June, you all had a meeting on Reg Guide 8.39. That's another important issue for us related to the issue of patient release. We heard from you that you thought we should emphasize the major source of radiation dose to individuals will be from external exposure in the cases

of patient release. The comment period for that Reg Guide is closing soon.

So, we'll be taking your input as well as what we get from other stakeholders, and moving to a finalized Phase 1 of that Reg Guide. As you know, Phase 1 really focuses on patient release instructions, which has been an important issue for the Commission and the staff. And then, we'll move into Phase 2 of the Reg Guide, which will look at more of the dosimetric calculations underlying patient release and the assumptions that go under that. And that will be another important part of our work.

Just back in July, you all met to help us work through, once again, the issue of our abnormal occurrence criteria. We have been asked to relook at that again by our Commission recently this past spring, and we heard your feedback, that you do feel like the AO criteria for medical events needs to be reviewed and revised. We are working on a SECY paper that will go to our Commission to ask for their direction on that issue. And we've taken into account what we heard from you back in July.

A couple of updates on NRC organization. It's certainly hard to keep track of these days. There's a lot of changes. But one that does impact

you, the office that our Division resides in, the Nuclear Materials Safety and Safeguards Office, will be reorganizing in the middle of October. It won't impact this Division where medical responsibilities lie. We are combining two other Divisions, the Division of Fuel Cycle and Division of Spent Fuel into one Division. I will be moving over into that Division, starting October 13th. And then, Mike Layton, who is currently the Director of our Spent Fuel Division, will be moving into this position over materials safety and medical issues. Kevin Williams, whom you've probably met over the years, who is my Deputy, will continue to be the Deputy of the Division.

An update on ACMUI member changes. This is Dr. Palestro's last meeting. I wanted to take a minute to thank you for your time, effort, dedication to your work on the Committee over eight years. That's a long time and a lot of important issues have come across for your consideration over that time.

This afternoon, our Chairman, Chairman Svinicki, will be here for a special presentation to you. So, we're looking forward to that and to thank you for your service on the ACMUI.

As Chris mentioned, a special welcome to Dr. Hossein Jadvar and Gary Bloom, who are new members

to the ACMUI. Dr. Jadvar was selected, as Chris mentioned, as the Nuclear Medicine Physician Representative, and Mr. Bloom was selected as the Patients' Rights Advocate Representative. So, welcome. And I just wanted to reiterate what Chris said. We do encourage you to participate and thank you for taking the time to be here.

Lastly and importantly, Dr. Darlene Metter and Dr. Robert Schleipman have been selected as ACMUI Chairman and Vice Chairman, respectively. They will assume these roles on September 23rd, at the end of Dr. Palestro's term.

And then, just a couple of highlights for the meeting over the next couple of days. I mentioned the T&E presentation that we'll have this morning. We're going to hear from some of the subcommittees that have been working hard on a number of issues. We're going to hear from Dr. Ennis on the Subcommittee's results of the FY18 review of medical events. We'll hear from Mr. Green on the Subcommittee's recommendations on extravasations. And finally, we'll hear from Dr. Wolkov to discuss the Subcommittee's recommendations on the Xcision GammaPod licensing guidance that I know has been on everybody's mind.

And then, just to highlight for tomorrow,

tomorrow we're going to hear from an individual from the National Nuclear Security Administration, who will be talking about their efforts to enhance security of radioactive materials and the use of alternative technologies, which I know has been an issue for quite some time.

And then, just one of my personal favorites, we're going to talk about emerging medical technologies tomorrow. The reason I mention it's one of my personal favorites is, as you know, the NRC has been looking at how we can transform our regulatory approaches. And one of the reasons we are looking at that is because in some cases our regulatory infrastructure doesn't accommodate new technologies very well. And, of course, there are new technologies in medical all the time, as you know.

And one of the things that we have tumbled to in the last year or so is that, as a regulatory agency, we really need to be in the forefront of seeing what new technologies may be coming our way, so that we can take the time to prepare for those and understand them. So that we can provide timely feedback on those technologies and not be an inhibitor on the use of those technologies for the benefit of patients. So, I'm very glad to see that on the agenda. It's very important

to us. And I'll be listening with a keen ear.

With that, I'll turn it back over to Chris.

MR. EINBERG: Or to Dr. Palestro.

MS. KOCK: To Dr. Palestro.

CHAIRMAN PALESTRO: (presiding) Thank you very much.

The next item on the agenda is old business and it will be presented by Ms. Jamerson.

MS. JAMERSON: Good morning.

I'm seated to the side. Can you all hear me okay?

So, this is the part of the meeting where we review all of our open and/or pending recommendations or actions that come from the ACMUI.

At our last ACMUI meeting in the spring, the NRC staff took back the action to review the ACMUI open action items and recommendations, ranging from 2007 to 2019.

A memorandum was issued to the Committee on August 23rd which detailed how each item was dispositioned and/or provided a path forward for some items and a resolution.

So, at this time, I'm going to go through the items on the chart. On the screen you will see the chart for 2007. Items 33 and 34 were related to

35.491, and from the memo, these two items were not accepted. And this is related to -- they were not included as part of the January 2019 revision to Part 35.

For the 2008 chart, for Items 19, 26, and 27, these are also outlined in the August memo. For Item 19, it was partially accepted by the staff, and there are several subsections to this justification and the response in the memo. For Item No. 26, it was not accepted by the staff. Item No. 27 was also not accepted by the staff. And again, there is further explanation in the memo that was provided.

For the 2011 chart, Item No. 6, this action item was accepted. And to note that the staff plans to revise our internal policy and procedure to incorporate this recommendation.

2008 -- I'm sorry -- 2016, for Item No. 16, the status has been closed. Item 24, this item has been closed and we also plan to update our NUREG brochure 0309, and it has an anticipated completion date of January 2020.

For Item 39, this item has been closed, and this item is currently going through our internal concurrence process and should be issued with a target date of December of 2019. For Item 42 and 43, well,

39, 42, and 43 are related to the Y-90, and they all have been closed with a target completion of December 2019.

For items 44 through 53, related to the NorthStar guidance, there was a separate memo that was issued on July 10th, 2019, to the ACMUI that outlines the path forward for these items.

And I'll just go through. So, Item 44 was not accepted. Item 45 was accepted. Forty-six, 47, 48 were not accepted. Item 49 was accepted. Item 50 was partially accepted. Item 51 and 52 were not accepted, and Item 53 was accepted. And again, these recommendations and the NRC staff responses were provided in a memo dated July 10th.

For 2017, for Item 13, this was captured, also, in the August 23rd memo, and it was not accepted. Item 14 was partially accepted. Item 15, 16, 17, 18, 19 were also not accepted. And Item 20 is still pending. The staff has decided, at a later date, to determine whether to include the patient intervention recommendations. So, this item is still pending. And as I stated, these items are -- there's more information or more details about the staff responses in the memo.

For the 2018 chart, for Item 1, this item was accepted and closed, and these will be updated in

the staff's Reg Guide 8.39. And we have a target completion date for that for April of 2020.

Item 2 was also accepted. Item 6 was accepted and Item 7. These will also be included in the update to our NUREG with a target completion of December 2019.

For Item 11, this item was accepted. Item 14, accepted. Item 15, the recommendations that were provided by the Subcommittee for the Germanium-68/Gallium-68 licensing guidance, this was also captured in a separate memo. And all those recommendations were accepted by the staff. And this is dated August 22nd. And Item 16 was accepted and also closed.

Items 17 through 19 were accepted and closed. For Item 20, this information notice has been drafted and is expected to be issued next month, October 2019.

MR. EINBERG: I would just add a note that that was just issued this past week. So, at the next meeting we'll close that.

MS. JAMERSON: For the 2019 chart, so Items 1 and 2 are related to the training and experience requirements. As has been mentioned, this is one of our items that is going to the Commission and we are

preparing an options paper for it. So, these items have been accepted with a target completion date for December 2019.

For Item 3, this has been accepted with a target completion of December 2019. Item 4 has been accepted and closed, and we will hear more from the Subcommittee today. Item 5 has been accepted and closed. Item 6, regarding the ACMUI Bylaws, those changes have been accepted and closed. And just to note that the Bylaws were revised as of July 2019. Item 7 has been accepted and closed. And we will hear from NNSA tomorrow. Item 8 has been accepted and closed. Our opening remarks have been revised and now reflect the conflict-of-interest statement. Item 9 has been accepted and closed.

And if you note from the presentation of the old business, you will see that we have incorporated a column to note our staff's target completion dates for these action items.

Item 10 has been accepted and closed. We will also hear from the Institutional Memory Subcommittee at this meeting. And Item 11 has been accepted and closed, and we are convening this meeting today, September 10 and 11.

For Items No. 12, 13, and 14, these are

a result of our summer meetings. For Item No. 12, this relates to the Bylaws, the changes that were presented. And as I mentioned, the Bylaws are now revised and have been posted as of July 2019. Item 13, Reg Guide 8.39, the Subcommittee report, the ACMUI endorsed the report and all the recommendations provided therein. And Item 14, from our July 24th teleconference, the Committee recommended that the NRC's medical event abnormal occurrence criteria needed to be reviewed and revised.

And so, for these three that remain open, do I have a motion to close these items? Yes?

CHAIRMAN PALESTRO: So moved.

VICE CHAIR METTER: I second.

CHAIRMAN PALESTRO: Any discussion?

(No response.)

All in favor?

Any opposed?

Unanimous.

MS. JAMERSON: Thank you.

CHAIRMAN PALESTRO: Thank you, Ms. Jamerson. I appreciate the efforts that you've carried out over the past several months to tidy up this list that goes back to, in some cases, 12 or 13 years.

I have a question. The items that are

closed, will they now disappear from this list?

MR. EINBERG: Well, I believe the answer is, yes, that we maintain those records for it.

CHAIRMAN PALESTRO: Okay. That's good.

The second question I have is, in this list it was noted and agreed that the statement about conflicts of interest would be included at the beginning of every meeting.

MR. EINBERG: Correct.

CHAIRMAN PALESTRO: Did we include it at the beginning of this meeting?

MR. EINBERG: It was included.

CHAIRMAN PALESTRO: I'm sorry, I didn't hear that. Thank you.

(Laughter.)

Thank you. All right.

Next, we move on. The next item is the open forum to identify medical topics of interest for further discussion.

Are there any topics that anyone would like to bring up?

(No response.)

I have a topic that I would like to address at this time. As you know, we have the training and experience for all modalities Subcommittee that is an

ongoing subcommittee. And at the present, Dr. Metter is Chair of that Subcommittee. However, under the change in the Bylaws, which I think was an appropriate change, it clarified issues regarding the role of the Chair of the ACMUI. It was decided that the Chair of the ACMUI could, in fact, serve on a subcommittee at the invitation of that subcommittee, but could not serve as the Chair of that subcommittee.

And in a matter of 10 or 11 days, whatever it is, I will be stepping aside, and Dr. Metter will be assuming the role of Chair of the ACMUI, which precludes her from continuing to serve as Chair of a subcommittee. And that's somewhat unfortunate with the timing because of the fact that there is a report due from that Subcommittee as of sometime, I believe, in early October. So, in order to ensure a smooth transition and to make sure that the report is thorough and completed on time, having discussed it with both Dr. Metter and Dr. Schleipman, Dr. Metter will step aside as Chair of the Subcommittee the day she assumes Chair of the ACMUI, and Dr. Schleipman will assume Chair of that Subcommittee. And again, it will be up to the Subcommittee to decide whether or not the Chair of the Committee should be invited to serve on that Subcommittee.

Any questions on that?

MEMBER SCHLEIPMAN: I think most of the Subcommittee is here. We would certainly, speaking for myself, would certainly welcome Dr. Metter's continuation and her experience. I think we would profit greatly from her being on that committee.

CHAIRMAN PALESTRO: Mr. Einberg?

MR. EINBERG: Yes, I would also note, once you rotated off and Dr. Jadvar is available, he could serve on the committee, if invited by the Chair of the Subcommittee.

CHAIRMAN PALESTRO: Mr. Ouhib?

MEMBER OUHIB: Yes, just a comment on that. Would it be possible, to avoid these situations, to simply state that, if the person was serving prior to, they should be allowed to continue? Because that was prior to being the Chair of this Committee. It's just for continuity I think it would be desirable, in my opinion, because that Chair is very well aware of what that committee is actually doing. Just a thought.

CHAIRMAN PALESTRO: My response to that is that the Bylaws Subcommittee looked at that, and the conclusion that they came up with, for a variety of reasons which they enumerated very clearly in their report, that while the Chair of the ACMUI could continue

to serve on the subcommittee, they could not serve as Chair of that subcommittee. And those are the rules in the Bylaws as of now. That, of course, does not preclude the formation or reformation of a Bylaws Committee at some point in the future to go back and revisit that.

Any other comments or questions from anybody in the room?

(No response.)

No? Hearing none, then the next item on the agenda will be the Training and Experience Evaluation. And Ms. Ayoade and Ms. Lopas will present.

MS. AYOADE: Thank you.

Can everybody here me okay? Yes? Okay.

So, good morning, everyone.

My name is Maryann Ayoade. I am the technical lead for the Training and Experience Requirements Evaluation Project that we have been conducting.

As you are aware, late in 2017, the Commission directed the staff to take a look at the training and experience requirements for radiopharmaceuticals under 10 CFR 35.300.

Next slide.

And so, today I will be providing a status

update on the staff's evaluation thus far. I will be going through the options that the staff has put together in the Draft Commission Paper, in the draft to the Commission, and I'll be outlining the next steps of the evaluation.

Next slide.

So, since the ACMUI September 2018 meeting, the NRC staff has been implementing the Stakeholder Outreach Plan. And that involved conducting several public meetings, as well as attending some professional society meetings to inform them about the ongoing project and to get some feedback and comments as well.

We also received input from the medical community at large and the Agreement States via two public comment periods. The last ended in July. And we also received input from the ACMUI as well.

Since then, the staff has developed a Draft Commission Paper that provides options regarding the NRC's training and experience requirements.

Next slide.

So, what is some of the feedback that we have received? From the medical community, the nuclear medicine and radiation oncology communities, which are the primary types of physicians that we see that use these medical radiopharmaceuticals under 35.300, they

strongly support maintaining the status quo. So, they want to maintain the current training and experience requirements under 10 CFR 35.300. And they also have opposed any revisions to the requirements that would tailor the requirements to create new limited Authorized User pathways.

We also heard from some non-traditional physicians. So, those are like your medical oncologists that are looking to treat patients with patient-specific-type radiopharmaceuticals that we're starting to see more of now. And they support the tailoring of their training and experience requirements to tailor the training hours from 700 hours to 80 hours of training and experience.

Next slide.

We also heard from the Agreement States. The Organization of Agreement States and some states oppose any tailoring of training and experience. The OAS and some other states also suggested that the NRC and the states should no longer be involved in the review and approval process for the training and experience for physicians; and that the NRC should, rather, rely on other entities to credential the Authorized Users. Other entities they referred to as the medical specialty boards. They want them to be able to

credential their physicians to use radiopharmaceuticals.

They also commented that the current training and experience requirements are not necessarily aligned with the NRC's Medical Policy Statement.

Next slide.

So, what are the training options that the staff currently has in the Draft Option Paper to the Commission? They generally fall under two approaches. The first approach would provide options that would revise the T&E regulatory framework to remove the current prescriptive requirements, and the NRC and Agreement States would no longer be involved in the process of reviewing and approving the training and experience for Authorized User physicians.

The second approach, that would provide options that would maintain or enhance our current, existing regulatory framework.

Next slide.

So, under Approach 1, the first option is the specialty board credentialing option. And this option, physicians must be certified by any medical specialty board. So, it wouldn't have to be one of the NRC-recognized medical specialty boards. It could

be any other type of specialty boards than what we see currently, which for 35.300 we see, we approve or we recognize the ABR, ABNM, and AOBR.

We also have the second option, which is a licensee credentialing option. And under this option, licensees would develop their own policies and procedures for credentialing their physicians.

And the third option is the NCR-recognized specialty board credentialing, where physicians must be certified by a medical specialty board that has been recognized by the NRC. But, rather than the current requirements that we have right now for recognizing medical specialty boards, it would be something more of a higher level for the board certification criteria.

And so, as I mentioned, the NRC would be providing higher-level requirements in the regulation for certifying physicians as Authorized Users, and the NRC would also be relying on other organizations to approve the Authorized Users, in accordance with a written directive -- I mean, in accordance with the requirements.

The Authorized Users would still maintain responsibility for ensuring that the prescriptions are in accordance with the written directives and, also, there would be regulatory emphasis on performance-based

inspections to ensure safety and security of the radiopharmaceuticals; and also, to make sure that they are effectively handling the radiopharmaceuticals. Also, this approach could be applied to other sections of our Part 35, so other medical uses in Part 35.

Next slide.

So, the second approach provides options that would maintain or enhance the current regulatory framework. And so, the first approach would be to maintain status quo, so it would keep the requirements as is. There would be no changes.

The second approach, or the second option would be to tailor the requirements. And so here, the training and experience would be tailored and reduced for use of individual radiopharmaceuticals or for categories of radiopharmaceuticals. And this option would also create additional Authorized User pathways.

The third option, the emerging radiopharmaceuticals option, this is for individual reviews of each radiopharmaceutical as they come down the pike to determine any drug-specific training and experience requirements or any type of requirements that we see fit. And it would be somewhat similar to what we currently have for the regulations for our new and emerging technologies under 10 CFR 35.1000.

The fourth option is the team-based requirement option. And here, the training and experience, it would be reduced based on pairing Authorized Users with other individuals with radiation safety training. And at a minimum, the team would consist of an Authorized User, a technologist, and a Radiation Safety Officer.

Next slide.

So, what are the next steps in this evaluation process? Currently, the ACMUI T&E Subcommittee as well as the Agreement States are reviewing the Draft Options that we currently have to provide to the Commission. And so, we gave that to them in August, and their comments from the review are due to us in October. So, for the ACMUI T&E Subcommittee, the comments are due to us October 7th, and for the Agreement States, the comments are due back to us on October 18th.

We also plan to have an ACMUI public teleconference on the comments from the T&E Subcommittee, and that is currently scheduled for October 17th. Yes, so that's scheduled for October 17th. And during that teleconference, we'll hear from the full Committee on feedback and comments from the T&E Subcommittee's review and recommendations.

Following that, staff will work on finalizing the paper to the Commission and we will consider the comments that we receive from the Agreement States and the ACMUI. And we will use that to inform our paper, our Commission Paper, in November and December, with our goal to deliver the paper to the Commission by December 20th of this year.

And I believe that's it. Yes. So, I'll take any questions the Committee may have.

MEMBER SCHLEIPMAN: I have a question. Could you go back to the Approach 1, the Option 1C, "Recognized Specialty Board Credentialing". And perhaps for the benefit of everyone who is here, describe in a little more detail what you meant by "high-level board certification"?

MS. AYOADE: Yes. So, right now, the NRC's criteria for recognizing medical specialty boards is based on the training and experience requirements for each section. So, for example, an Authorized User that wants to use 35.300 uses, they would have to be board certified by the recognized boards, which are listed on our website.

And those boards, they submit an application to the NRC saying that they meet all of our current training and experience requirements. So,

that would include our training topics that are listed; the prescriptive 700 hours, including classroom and laboratory; the casework experience. So, that's what that involves.

And for this, we are looking into something of a more high level. Probably we are looking at listing topics and certain things that they have to meet at a minimum, but not nearly as prescriptive as what we have now.

CHAIRMAN PALESTRO: Dr. Metter?

VICE CHAIR METTER: Thank you.

That was my question, too. I also would like to ask, they could have the training and experience, but is there going to be a method to address competency? Like is there going to be an exam, then, for Option 1C? Or a sort of assessment of did that individual attain the knowledge and skills required for an Authorized User for that radiopharmaceutical?

MS. AYOADE: Yes, I would say that that is something that we have considered for these options. But, as of right now at this stage, as we're presenting it as an option, those details can be fleshed out after the Commission moves forward with picking one of these options. And we can flesh out some more. We've had a lot of discussion as to whether examination should

be involved, but right now we haven't put it down as a "set in stone" for each option, which ones would involve exams or not. And we would be getting input from you guys as we move forward, when we go into -- if it ends up going into a rulemaking phase or anything of that nature.

VICE CHAIR METTER: Thank you.

MS. KOCK: Just at a really high level, I think -- I mean, I'll try not to reiterate exactly what you said -- but this is so really complicated. So, I think we started out with like 15 options. I mean, there's so many different iterations of these different options that you could think about and including should there be some kind of competency testing. And so, just to simplify it, I think what we're trying to accomplish with the paper is just get the general direction from the Commission.

And that's why we broke it into approaches. Approach 1 is more of a radical rethinking of the way we do T&E. And Approach 2 is more enhancements in what we currently have. And things like should there be competency modeling, the specific makeup of a team approach, if we go with a team approach, are details that we work out after we get Commission direction.

So, I think our goal for the December paper

is just to get the general direction, and then, we would have stakeholder interactions to work out the details.

VICE CHAIR METTER: And the only reason I ask that, too, is that you have different options. You have three. And I would like to understand what is the goal for all of them. Is that to have equivalent assessment and assessment of competency at a national level, so that it's a uniform standard throughout the country? And that's what I would suggest when you go through Approach 1.

MS. AYOADE: Okay.

MS. KOCK: But I think at a high level, to address your point of uniformity, that's one of the considerations between these different options. So, licensee credentialing, we would be leaving up to licensees to determine their own policies and procedures for how they credential, which wouldn't bring uniformity. But Option 1C would bring more uniformity because the NRC would have some criteria. It would be very high-level and performance-based, but it would set the standards for some uniformity. So, that's actually one of the considerations that we'll need to look at, yes, exactly.

CHAIRMAN PALESTRO: Mr. Ouhib?

MEMBER OUHIB: Yes, to follow up on that,

it's on Option 1B, "Licensee Credentialing". So, the licensee will develop their policies and procedures. Wouldn't that create some sort of inconsistency throughout? And going back to the standard, now we're faced with a variety, and that could potentially bring some issues.

MS. AYOADE: Yes, so we plan to have, at a minimum, some high-level -- like I mentioned for the last option, and it would apply to all these options really -- we would have each option to some extent meet some radiation safety requirements for NRC as it applies to each option. But, then, we leave it up to the licensee for that option to develop the details of how they want to apply it, and we would review it. It's kind of similar to what we do for the medical broad scopes somewhat, where we have the basics that they need to meet, but how they meet that, they'll submit that to us and we'll review that to see if it's something that's acceptable or not.

CHAIRMAN PALESTRO: Dr. Metter?

VICE CHAIR METTER: That's an interesting concept which I think is a good proposal for an option. But I'm wondering about, there are thousands of licensees, and I would just wonder what workload would then be placed on. It's just a comment. It's just

a comment.

MS. AYOADE: And I'm glad that you're bringing that up. We did consider for these options which are provided to the T&E Subcommittee the pros and cons of these options. And there are pros and cons, and that's one of the cons for this option, as you mentioned.

VICE CHAIR METTER: Thank you.

CHAIRMAN PALESTRO: Dr. Ennis?

MEMBER ENNIS: A couple of thoughts. So, first, I just want to commend the NRC for the openness of thinking outside the box and creatively about other options. It's nice to see.

As I keep thinking about these, some of these are a little hard to interact because they're a little big, which I guess is intentional at this level, but it makes it a little hard, for me at least, to kind of assess and advise.

But I would say that I think there is a consensus among NRC and ACMUI that the current regulations are very safe.

MS. AYOADE: Yes.

MEMBER ENNIS: And although we have events, and I'm on the committee that tries to figure out ways to even minimize those further, for the

millions of procedures done per year, the number of events is low. And I think the NRC deserves a lot of credit for that.

And there's so much misperceptions about radiation in the community at large, and the physician community, in particular, that, if not for that, we would either have a lot of events going on because of a lack of understanding of the issues involved. It's not there and it can be so misperceived as safe. And on the other hand, the other extreme also exists of people, especially in the lay public, being so afraid that they would deny themselves lifesaving care and imaging because they're afraid of the radiation. But the community at large feels comfortable that the NRC is regulating this and is comfortable doing that.

And I don't think we should minimize both sides of the ways it could go and the skill with which the NRC over the decades has really managed to keep the ship going well, where the lay public feels relatively safe, and our results have been safe.

In trying to think about going different directions, to me, the crucial question is, all right, what aspects of the current regulations are the core ones that are really working and which are the ones that may be superfluous and just over-burdensome

regulatory? And I don't think we've really asked that question or answered that question. And without an answer to that question first, I think it's potentially very dangerous, one way or the other, to move forward with some of these directions which seem to be -- each one has a rationale for it. But, without like a good basis, in my mind, of like, okay, these are really the core elements that we're sure make it safe -- so, I would suggest, I know the Commission wants a paper soon, but I just have a lot of concerns that each of these have potential areas of significant lapse.

Because the more we leave it to people without radiation expertise, which is what a lot of these things are trying to do, loosen things up a little bit -- you know, the underlying implication is it's over-regulatory and we don't really need to be so strict because it's so safe. But leaving it up to people who don't have a good expertise, or a good knowledge of safety culture in general or it's not been their expertise, to understand, okay, what are the core elements that are really important, it feels to me that that would be really premature to run ahead with a recommendation of any of these without a further vetting of, okay, what really are our core things? And then, once we've identified those, then maybe we can be

creative about solutions.

But, right now, as I say, many of these give me a lot of anxiety because, as I say, other medical specialty boards, for example, it's not really possible for them to come up with regulatory -- I mean, they're great at what they do, but they don't know anything about radiation. They might want to use it, but they don't know anything about it. And even the people in that board who would want to make it safe -- I don't mean people who are just trying to scam the system, but people who genuinely want to do, but don't have the knowledge or the capability.

And how would that happen? Licensees, again, the comments about that -- we could go through each one, but that was the point I wanted to make.

MS. AYOADE: Yes, thank you for your comment, and I'm glad that you brought that up. I just wanted to also add that we're at a time where there is a lot going on in the radiopharmaceuticals. We're seeing emerging technologies that we're not too familiar with in terms of the procedures and processes that are involved, the team that it takes to handle the radiopharmaceuticals. Possibly looking into the type of supervision that we have for radiopharmaceuticals, which are different from what

we have for the other modalities.

And so, this project came at a time where the ACMUI has also set up a subcommittee to periodically look at training and experience in general for our training sessions. But, then, also, this project came up to focus on radiopharmaceuticals. And so, I thank you for bringing the comment up, and I want you to know that we're considering that strongly, and we tried to do the best that we could in focusing on this project as well.

CHAIRMAN PALESTRO: Mr. Ouhib?

MEMBER OUHIB: Just curious, again, going back to 1B, could that be not left up to a licensee, but perhaps to practice guidelines sort of that are established?

MS. AYOADE: Okay.

MEMBER OUHIB: And that would be to be followed by just about everybody pretty much.

MS. AYOADE: Okay. Thank you for your suggestion. We'll take that into consideration.

CHAIRMAN PALESTRO: Dr. Jadvar?

DR. JADVAR: Thank you, Dr. Palestro.

First of all, I'm very glad to be joining this panel.

I have a question. It looks like, except

Option 2A, which is the status quo, the other options, it seems to me that the underlying reason for considering any of these options, except that particular option, 2A, is that there is a perception of a shortage of current or anticipated AUs to deliver what is available right now or what is emerging. And you targeted radionuclide therapies. Is that actually accepted as a fact, and that's why you're considering all these options?

MS. AYOADE: Actually, no, it's not accepted as a fact. It is one of the items that came up as part of this evaluation, but it's not the only thing that is the underlying issue. Again, like I mentioned, it's been a while, like the ACMUI discovered, since we reviewed our training and experience requirements at large.

And then, there's other emerging radiopharmaceuticals coming down the pike, that NRC needs to pay attention to other parts of the regulations that may need change and may be affected. As I mentioned, one example is the supervision requirements, and possibly maybe looking at requirements for the type of individuals that are involved in the procedures as well. So, it wasn't just the patient access issue, but it was something that we looked at as part of this

evaluation.

We reached out to the Agreement States because they're a large part of our regulators -- it's not just NRC licensees -- to try to get information and data. And you'll see that as part of our paper. We have a section that discusses the data that we got from there. But, right now, that is not something that we said is the moving or driving factor for the options that we have.

DR. JADVAR: I have one followup question. So, I think I saw 80 hours somewhere in one of these slides.

MS. AYOADE: Yes.

DR. JADVAR: So, this just seems very interesting to me, that suddenly we're going from 700, which is the current status, to 80 hours, which is almost 10 percent. So, basically, that means that, let's say, a medical oncologist can go and take a couple of weekends or perhaps even an internet-based course --

MS. AYOADE: Yes.

DR. JADVAR: -- and, then, start giving radioactive material to people, to patients. It's just kind of, as I said, just very interesting.

Is it possible for me, as a nuclear medicine physician, to go and take a couple of courses and, then,

start giving people chemotherapy in 80 hours of training? I mean, this is something that I think we need to discuss.

MS. AYOADE: Yes. Thank you for your comments.

CHAIRMAN PALESTRO: Yes. This is Dr. Palestro.

Dr. Jadvar, that discussion has come up numerous times over the past couple of years, about the number of hours, whether it should be 80 or 700, or some other number. And in point of fact, if you go back over many years, as we've tried to do, you'll find that there's no basis in fact or justification really for any of these hours. And I'm not suggesting that 80 is sufficient.

But I also want to point out -- and Ms. Ayoade and Ms. Kock, correct me if I'm wrong -- but what you have shown us here, and what you have written up and put in the slides, is a compilation of the various possible routes that the NRC could go?

MS. AYOADE: That's correct.

CHAIRMAN PALESTRO: And it's based on input from stakeholders, the ACMUI, the Subcommittee, and so forth; that you're not endorsing at the moment any of these recommendations.

MS. AYOADE: That's correct.

CHAIRMAN PALESTRO: This is a summary of what you think is the best representation of all the suggestions that have been made. And now, this summary and each of these options is out for commentary --

MS. AYOADE: Yes.

CHAIRMAN PALESTRO: -- both by the public, by the Organization of Agreement States, and, of course, by the ACMUI.

MS. AYOADE: That's true. And as Andrea mentioned earlier, we have been trying to be open with the public. And we had at some point 15 options or so. And we had public comment periods. We tried to push the rest of the community and the public to see what they can give us in terms of feedback, based on different options. And this is what we have narrowed it down to come up with, that we're putting forward right now to present to our Commission. But we're still going to take into consideration the comments from the ACMUI T&E Subcommittee, the comments from that public teleconference that we'll be having, and also the comments from the Agreement States that we're expecting to receive in October.

CHAIRMAN PALESTRO: My second question or comment on this is that, once you have gone through

all of the comments and the feedback and the input, and have decided what you feel is the best option that you're going to put forward to the Commission, will that option be detailed with all of the microstructure, so to speak, or will it be a general option with details to be filled-in in the future?

MS. AYOADE: Yes, it would still be a general option. We will put forward a recommended option, but we would have, also, all of the other options that we feel -- like some of these, they may still make it in there, or they may not, based on the comments that we receive from you all and the Agreement States.

But I believe Andrea mentioned it earlier. The details are not going to be fleshed out. It's just going to be the general concept of what the option is going to look like. Because in order to flesh out the details now, we would have to take a look at -- I mean, there would have to be a whole lot more effort in terms of the rulemaking, the cost-based analysis, and things of that nature as well, and how it's going to affect our other regulatory counterparts.

CHAIRMAN PALESTRO: My last question is, once you have formalized your recommendation, will the ACMUI have an opportunity to review it or to see it before it is sent to the Commission?

MS. AYOADE: No. We want to do our best in making sure that we don't give the ACMUI biased opinion as they move forward and they give us their options. And so, right now, no.

CHAIRMAN PALESTRO: Got you.

MS. AYOADE: We won't be presenting our recommended option to the ACMUI.

CHAIRMAN PALESTRO: Any other comments or questions from the Committee? Anybody in the room?

MEMBER ENNIS: So, you were asked whether a potential perceived shortage of AUs was accepted as fact. You said it was not. But would you be willing to share whether the NRC staff thinks that's likely to be correct? Like to what degree does the NRC think that that is somewhat or very much a problem or not a problem at all? Like what's your perceptions?

MS. AYOADE: Yes. So, I'll call on Sarah because she was a big part of manning the project that included us taking a look at the data that we received and some of the comments that were received, including numbers for the current positions in the different parts, the different states that we got.

MS. LOPAS: Hi. So, I'm Sarah Lopas. I've been working with Maryann on T&E. I'm a Project Manager.

So, we did not make a conclusion on whether or not there is a shortage. We pulled data from our licensees, from the web-based licensing system. We did our best to pull the number of AUs when it wasn't a broad scope licensee, the number of full AUs even, so not even just the AUs that are limited to like I-131, right? We wanted to see what are the number of AUs that could provide any kind of radiotherapy, right? So, that, of course, only gives us about 13 states and Puerto Rico, or something along those lines.

And then, we did a voluntary request for information from the Agreement States. And Wisconsin was one of those states that provided data for us. And it was a voluntary request, because if we had made it mandatory, it would have been a 12-month approval process to get that through to make that mandatory request.

And I believe we got 13 states, Agreement States, that provided us their data. Not all states gave us their AU data. So, we literally just got locations of facilities that had a 300, an AU that could offer a full 300 use at that facility.

So, we have maps that we developed that kind of just show the distribution. I mean, and it's not surprising, the distribution of these facilities

with these AUs is in more populous areas. That's kind of a fact of life of any kind of complex health care, right?

So, we're just presenting that information for folks to take a look at. We did not draw any conclusions. We don't know what is enough AUs, right? And we take your information that you put forward in your report saying, you know, we listened to the medical community; we listened to you all; we listened to the Agreement States, on whether or not they feel there are enough AUs to meet the demand for these therapies.

And I think as you all discussed in previous meetings, there's lots of reasons why maybe some of these therapies aren't being used as much as they thought, that aren't just limited to the availability of an AU.

So, to answer your question, long story short, we do not make a conclusion with regard to whether there is a shortage or whether we need more. So, it did not drive our evaluation. It was considered, but it's not going to drive our recommendation, if that helps.

CHAIRMAN PALESTRO: Dr. Ennis?

MEMBER ENNIS: Just as a followup, again, I'm trying to put myself in your shoes and understand

what the motivations are, besides just being flexible, and every once in a while reconsidering things. And that may be what it is.

But, I mean, is there a concern that, with a lot of new potential agents coming out, as many of us are hearing, that the NRC would just like be overwhelmed from their own work point of view, having to regulate all those, and therefore, want to simplify it, so they don't have to spend the time and energy regulating that? Is that a concern? And to what degree is that a concern, if it is?

MS. AYOADE: I mean, I would say, again, that was not something that was a driver for this. But, again, as we considered the different options under each approach, that's something we have to consider. You know, there are different pros and cons to each option, and it's not just NRC; we have to also take into account our regulatory counterparts as well. And so, yes, that's something we did consider, but I wouldn't say it was a driving factor for this project.

MS. KOCK: I think, Dr. Ennis, actually, what you were saying before is actually the driver. What is needed from a regulatory perspective? What should we be looking at? So, this is the age-old question from the Medical Policy Statement of what is

the NRC's appropriate role? I mean, I think you stated it very eloquently. Our role is to make sure from a radiation safety perspective that medical procedures are implemented in a way that assures radiation safety. And our role is not to get into the practice of medicine. And so, that is really what we're trying to sort out here. Where is the right line in the sand in terms of where we should set training and experience requirements? How much radiation safety training is needed? What is the NRC's role?

We've heard time and time again through history that perhaps in the area of training and experience is an area where we should have less of a regulatory hold; and that we are crossing the line when you look at the Medical Policy Statement. Some folks have said that.

And so, that, to me, is really the question. How much is needed? And I think we've heard from some stakeholders that some of the new radiopharmaceuticals that are coming down the pike would be more appropriate for a limited training. You know, if you only want to administer one fairly -- and I don't want to use the word "simple" -- but less-radiologically-complex radiopharmaceutical, could it be appropriate to scope the training and experience requirements down? So,

I think those are the things, and I think you were articulating some of that earlier.

CHAIRMAN PALESTRO: Mr. Ouhib?

MEMBER OUHIB: Yes, with the exception of Option 2A, which is the status quo -- and you can hear it probably; I do have concern on a lot of the other options -- do you have any system, or do you anticipate having a system in place to monitor in the event that, whatever option, instead of waiting and saying, "Oh, my gosh, I think we made a mistake here. What is going on? What do we do? How do we correct this?", and so on and so forth? In other words, have things in place that -- okay, how are we going to monitor this? What is going to happen? Have we made the right decision? Or we said that within two years -- I'm just speculating here -- if this does not seem to work, we have to fall back on whatever that might be.

MS. AYOADE: Yes, and I think those are some of the things that we have had a lot of discussion about. The option in Approach No. 2 would be enhancing what we currently have. So, it would be that the focus would be on Approach No. 1 options. And right now, we're looking more at the regulatory emphasis would be performance-based-type inspections. But, right now, those are things that we still have to consider.

As you said, if we move forward with one of the other options in Approach 1, what would we be falling back on? So, those are some of the things that we've been having a lot of discussions about.

CHAIRMAN PALESTRO: Mr. Sheetz?

MEMBER SHEETZ: I'd like to say I share Dr. Ennis' concerns. I think we need to answer the question, is there a shortage or are the current requirements overly-restrictive? I know the NRC is being challenged that they may be overly-restrictive, but it is the NRC's purview to ensure patient and public health and safety.

And I think you'll find, with the emerging technologies, which will be presented tomorrow, the options that are coming down, the new modalities coming down the pike are actually more complex. And it's not just a simple single administration and you don't have to worry about anything.

And so, I would be very cautious, and I think we have to be able to justify relaxing any current requirements and be able to justify that before we do so. It's going to get more complicated, not less.

MS. AYOADE: Thank you for your comment.

CHAIRMAN PALESTRO: Dr. Metter?

VICE CHAIR METTER: Yes, I would like to

reinforce Mr. Sheetz's comments, and just go back to what therapy is. For therapies to kill cells -- and the most hazardous radioactive material we have to do that is what we use, which are betas and alphas -- and to consider betas and alphas as the least dangerous, I think it's not really a correct approach. But I think that should be overarching. These are the most hazardous radionuclide materials that we use, and we use it for therapy, and therapy is to eliminate cells. And so, just to remind you of that. And so, the current status of medical events that have been reported and issued is because the individuals who are currently Authorized Users understand the hazards of alphas and betas.

MS. AYOADE: Okay. Thank you for your comment.

CHAIRMAN PALESTRO: Yes?

MR. PETERS: Hi. Mike Peters, American College of Radiology.

If you could just go back to the medical community feedback slide, whoever has control? This sort of implies an equal dichotomy of positions from the physician community specifically. As far as I know, the only comment submitted by someone supporting anything other than the status quo is from the American

Society of Hematology. The oncologists that you cited, as an example, voted to approve the AMA's position which was in support of the status quo. So, could you give a list perhaps of national specialty organizations that support anything other than the status quo? Thanks.

MS. AYOADE: I don't have a list on me, but Sarah may because she may have some of the comments in that Excel sheet. We tried to summarize the comments and present it here today, but we'll see if she has a list for you.

MS. LOPAS: So, this is Sarah Lopas.

As part of our SECY paper, we will be referencing an ADAMS number that is going to link you to a very voluminous comment summary report. It will show you all the commenters. It will summarize all the comments.

And I do think it's fair to say the first part of our comment, our first comment period, there were more folks in the status quo camp. The second comment period, it was a little more split, but I will say it was split by literally individual doctors coming in, right? And so, we had these medical oncologists and some folks coming in, urologists, individual doctors coming in, and some support.

And then, you, of course, had these large

medical communities, right, organizations that represent thousands, you know, thousands and thousands of doctors coming in support for status quo. So, I think that's a fair assessment.

In terms of groups that did come in, you're right, it was ASH, American Society of Hematology. We did have the American Medical Association come in. We had a conversation with them, and they supported status quo, but they ended their comment to us, which I thought was interesting, with that: you all should work with these boards, these other boards of these doctors who want to start being able to use these radiopharmaceuticals. And we thought that was an interesting comment. So, that was a little bit different, that reach out to these boards and see, and work with them to see if they can implement that training into some of their board programs.

I'm just taking a real quick look to see if there's anything else, any other large groups. CORAR, we did have some -- it was mostly kind of industry-related groups that came in and advocated for the tailored training experience.

MS. AYOADE: But we did want to make sure that we represented not just the group that we heard the most from for status quo, but to let everybody know

that there's other people that supported other non-status quo.

MR. PETERS: Right. Those instigated by manufacturers to come in and submit comments.

CHAIRMAN PALESTRO: Would you turn on the microphone, please?

MR. PETERS: I would suggest that perhaps a lot of those are folks that have been instigated by the manufacturers to submit comments. But certainly the national organizations, of them, ASH is the only one that I know of that supports a change. So, thank you.

MS. AYOADE: Thank you.

CHAIRMAN PALESTRO: Any other comments? Mr. Ouhib?

MEMBER OUHIB: Yes, I just have a followup. What Dr. Metter mentioned is that -- I would just like to caution you on there are currently within the AAPM, probably just as an example, there are some task groups being formed and there are some ad hoc committees, and so on. Really, the purpose is really to look at the dosimetry of these isotopes and, also, the imaging component, and to combine these to actually deliver a good treatment. Unless you are a center where you have this department that has these members that can

actually do all these procedures, I think we're looking for trouble. And that would be my take-home lesson.

MS. AYOADE: And I appreciate that comment. Again, one of the things that I mentioned is, as we were looking at some of the options, we were looking at other parts of our regulations as well, not just the T&E, that could affect training and experience. So, I mentioned the supervision or looking at the people involved, not just the Authorized Users. So, there's options where we looked at different kinds of teams with a minimum number of people. So, we considered the items that you mentioned as well.

CHAIRMAN PALESTRO: Dr. Jadvar?

DR. JADVAR: I just wanted to echo again what Dr. Metter said and what Mr. Ouhib just said. It is that there is no less-complex treatment. I mean, these are, as was mentioned, alpha particles and beta particles, and these are cytotoxic. These are it really takes a knowledge, a comprehensive knowledge to know to whom you should give it, what is all the things that goes around it. I mean, I'm sure these all have been discussed before. But I don't understand less-complex treatments. That, to me, just doesn't make sense. These are complicated, and you have to be trained to give something cytotoxic to your patients.

So, we have to be always cognizant of that. That is very important.

MS. AYOADE: Okay. Thank you for your comment.

CHAIRMAN PALESTRO: Any other comments? We have time for one more.

MS. COCKERHAM: This is Ashley Cockerham with Mercurie Consulting.

I actually thought of another question when Mr. Ouhib asked the question about how monitoring currently happens. And so, currently, NRC and the Agreement States inspect the licensees as part of a monitoring program. So, under Approach 1, where we would see these changes, would the NRC and the Agreement States continue to inspect as a way to monitor?

MS. AYOADE: Yes. But the type of inspections is what we're looking at changing. Maybe something like I mentioned before, it can be more performance-based, but with the goal of continuing to make sure that we're ensuring safety, security, and also effective handling of the radiopharmaceuticals as well.

MS. COCKERHAM: So, the Radiation Safety Program requirements kind of as a whole for the facility, for the licensee, those would remain in place?

Even though we're seeing a reduction for T&E, it's not a reduction in radiation safety or a reduction in the NRC's or the Agreement States' oversight?

MS. AYOADE: Yes, that's correct. So, the focus of this evaluation is really on training and experience with us continuing to enhance it as we see fit.

MS. COCKERHAM: Thank you.

CHAIRMAN PALESTRO: Ms. Ayoade, we're just about out of time. But if I could ask you to recap for everyone the dates --

MS. AYOADE: Okay.

CHAIRMAN PALESTRO: -- for each of the events that are going to happen between now and December?

MS. AYOADE: So, I believe that's the next slide. Yes.

And so, currently, the ACMUI T&E Subcommittee and the Agreement States still have the draft options. And so, they have until October, for the T&E Subcommittee, October 7th, and for the Agreement States, until October 18th, to provide their comments to us.

And then, the ACMUI public teleconference, where the full Committee will discuss the

Subcommittee's comments, and we'll also take in comments from the public, would be on October 17th. Yes, it would be on October 17th. So, the 17th is not on that slide, but we finalized the date. I confirmed with Kellee.

And then, after that, we will consider the comments from both the Agreement States and the ACMUI, and we would use that to finalize our options and our paper to the Commission. And we'll be doing that in November and December, with the goal to deliver the paper to the Commission on or by December 20th.

CHAIRMAN PALESTRO: Right. And then, I know it's getting ahead of ourselves a little bit, what happens next, once your paper has been delivered to the Commission?

MS. AYOADE: It's kind of I want to say, hands up in the air. It would be for the Commission to take the time I guess they need to review and provide us with instructions. Whether they pick the option that we recommend or they come up with something else, we won't know, but that is a time that we don't have right, is to say when they're going to deliver that to us.

CHAIRMAN PALESTRO: Thank you very much.

We're going to move on to the next topic

now, and then --

MR. EINBERG: Dr. Palestro?

CHAIRMAN PALESTRO: Yes? I'm sorry.

MR. EINBERG: Chris Einberg here.

I just want to remind you that the phone lines are open if you wanted to poll the phones to see if there's any public comments.

And then, before you choose to do that, I wanted to offer to the Subcommittee that the staff is available to meet with the Subcommittee to go into more in-depth discussions about the options, because there's a lot to deliberate for the Subcommittee. And so, please avail yourself of the staff, Maryann and Sarah Lopas.

CHAIRMAN PALESTRO: All right. So, then, I apologize for that, Mr. Einberg.

I will open it to anybody on the phone lines, if there are any comments on this presentation?

(No response.)

All right. Hearing none, we'll move on to the Medical Events Subcommittee Report. Dr. Ennis will present.

MEMBER ENNIS: Okay. Good morning, everyone.

This report will be relatively brief. So,

for starters, I want to thank my Subcommittee colleagues: Richard Green, Darlene Metter, Michael Sheetz, and Harvey Wolkov.

This Subcommittee meets annually, does a report annually, reviewing the medical events of the prior fiscal year. Just to refresh people's memory, up until a year ago, for several years in recent years, the Subcommittee essentially recapitulated, with slightly updated data, how it had done in the spring meeting.

And about a year ago, this Subcommittee decided, instead, to do a broader review over a four-year period of time to look at some themes. And last year at this time, the Subcommittee presented that and made some recommendations. I did, indeed, identify a couple of themes that could be advised, and then, ask the NRC to send out an information notice about that.

And as part of that, it was recognized that, given the relative safety that we had just alluded to before of the current system, and the relatively small number of events, to do such an in-depth analysis over a period of time with only one year's new data wouldn't really change things very much. And therefore, the Subcommittee would do the more in-depth analysis every

other year.

But, so as not to miss important emerging trends or new technology issues that would come up, we decided we would do a report annually, with the alternating years like this one being a less in-depth analysis, unless there was something important to report on.

So, with that as background, we'll go into the actual report. Next slide, please.

So, the table here showing the number of events by type. I'll give you a minute to look at it, but there's nothing really jumping out. As normal, things are fluctuating around. Some things have bumped up a little bit. Year to date compared to a couple of years, and other things have dropped down a little bit. But I think we could all agree that, basically, we're in the same ballpark. There doesn't seem to be any kind of an emerging trend that needed a deeper dive to anyone on our Subcommittee.

Next slide.

So, we did not identify any trends or emerging new issues this year. We look forward very much to next year doing a deeper dive over a four-year trend -- that will be two years of new data -- to see anything that's happening. It's probably still too

soon to see if any of our informational notices and advice are impacting any of the trends that we had seen or the themes that we had seen. That probably would take several more years, but we will start to look for that.

We did, however, in our discussions -- and this dovetails nicely with our prior conversation -- one potential new issue emerging, and again, this gets to the increasing use of radiopharmaceuticals, but, in particular, many of them that are coming, that are going to be coming, are of high activity and/or high volume of fluid. And both of those factors, especially both together, definitely increase the risks of MEs, and particularly ones of more serious consequence. So, that is something this Committee, this Subcommittee will be looking carefully at in the coming years to see if we see any trends, particularly about that.

And for the purposes of this report, that's the issue at hand. But, of course, this is relevant to the prior conversations that we just had, as comments have already been made.

So, that really concludes this relatively brief report for this year's analysis. But I'm happy to take any questions, and I do look forward next year to giving you a more in-depth analysis.

CHAIRMAN PALESTRO: Thank you, Dr. Ennis.

Any comments from the members of the Subcommittee?

MEMBER OUHIB: Yes, I have a question.

CHAIRMAN PALESTRO: Mr. Ouhib?

MEMBER OUHIB: I guess it's not just the high activity and high volume. It's also new treatment modality per se or a new radiopharmaceutical element, or something like that. Have you had a chance to look at, like going back and looking at other procedures and when they actually were brought into the medical community, what sort of medical events were occurring at that point right at the start? And this could be another alarming item to look at.

MEMBER ENNIS: That's actually a very interesting thought. We have not discussed that and we have not done that kind of analysis. Perhaps we could do that for one or two to try to identify what are the early trends of a new therapy when we do our next year's analysis. That's a nice idea.

CHAIRMAN PALESTRO: Any other comments or questions? Dr. Metter?

VICE CHAIR METTER: Regarding your comment, Mr. Ouhib, it would be like Y-90. When Y-90 first came out, within that first month they realized

there was a lot of medical event reporting. So, the NRC put out an information notice, I believe it was called, where if you had the Authorized Users state in the written directive the radiopharmaceutical administered activity or to stasis. And I think that, then, alleviated the medical event reporting that occurred at that time. So, there are things that do occur after particularly new modes of, methods of administration become available.

MEMBER OUHIB: Totally agree, and that's part of the unexpected or the things we didn't think about. All of a sudden, oh, my gosh.

CHAIRMAN PALESTRO: Mr. Green?

MEMBER GREEN: Yes, to follow up with Zoubir's comments, when Zevalin first came out, it was a first pure beta-emitting Y-90 radiopharmaceutical, and that brought up all the problems to come out of the woodwork on measurement and accuracy, dose calibrators, and NIST-traceable sources. And I think those have become accomplished for Y-90. There are new nuclides coming. There may be new bugs that come out of the woodwork.

To use brand names, with Quadramet, Xofigo, and Zevalin, the current intravenous drugs, they're all small volume, 10 milliliters or less. But with

Azedra and with Lutathera, we're seeing high volumes, high activities. And with Azedra, it's I-131. It's our good, old classic of the 1940s, a beta and gamma emitter. But, during this one cycle here, we do have a reported event of erythema from skin contamination.

But we'll have to look and see what comes. But we have a whole class of new drugs coming, and we're transitioning from the small volume, little bit of volume therapies, to big volume, big activity therapies, new classes.

CHAIRMAN PALESTRO: Any other comments or questions from the Committee?

(No response.)

Attendees here in the room?

(No response.)

Comments or questions from anybody on the bridgeline?

(No response.)

All right. Hearing none, we need a motion to accept Dr. Ennis' report.

(Moved.)

A second?

MEMBER SCHLEIPMAN: Second.

CHAIRMAN PALESTRO: Any further discussion?

(No response.)

All in favor?

Any opposed?

All right. Next on the agenda is a break. So, we will resume promptly at 10:45. Thank you.

(Whereupon, the foregoing matter went off the record at 10:10 a.m. and went back on the record at 10:46 a.m.)

CHAIRMAN PALESTRO: Call the meeting back to order, please.

All right. The next presentation is the Appropriateness of Medical Event Reporting Subcommittee Report, to be given by Dr. Ennis.

MEMBER ENNIS: Hello again.

Okay. So, an outgrowth of the prior Subcommittee, I guess probably a year ago also, led to discussions among the ACMUI at large and the Subcommittee, in particular, that looks at medical event reporting, and a growing feeling that it was hard sometimes to interpret the reports and make useful generalizations about the reports in our role of looking at medical events and helping the NRC create a safety culture, and things of that sort.

So, we formed a Subcommittee to just analyze, well, what are the requirements and what is

the process? And could we kind of articulate problems? Rather than just saying there are problems, and we get frustrated when we read some of the reports, could we articulate it in a way that's meaningful, and then, make some recommendations to improve on the problem that we were perceiving?

So, this Subcommittee was formed and we had a great team of Vasken Dilsizian; myself; Ms. Martin, who, unfortunately, is not here; Mr. Ouhib; Ms. Shober, and Ms. Weil, who, as all of you know, just rotated off, but she was also instrumental in many of our Subcommittee meetings. And Lisa Dimmick was a great resource for our Subcommittee as well.

Next slide, please.

So, as I said, our charge was to review the appropriateness of the current requirements, the required elements of the medical reporting, the adherence to these requirements, and recommending actions to improve the reporting.

Next slide.

So, we presented some preliminary observations and recommendations in the spring meeting. And now, we will provide our final report.

Next slide.

Just as background, one of the key purposes

of reporting is noted here, a lot of verbiage here. You can just look at the blue, italicized parts. A key element of a medical event report is to be able to assess trends, recognize inadequacies in equipment and procedures, to aid in the understanding of events, and try to prevent them from happening again. So, with that as background, we took that charge and looked at the current state of medical event reporting.

Next slide.

Okay. So, everyone I think is aware, NMED is the online, the web-based system, where the medical events are reported, either directly to NRC or through the Agreement States, and are governed by a bunch of rules. And that is what we use as our resource, and Donna-Beth uses as her resource, so the NRC staff uses as well, for viewing what type of medical events have occurred.

Some of the observations we made about NMED is that the narrative, which is really key to understanding what happened in many of these events, is inadequate for an ACMUI reviewer to actually understand what happened, to understand the cause, the contributing factors, as well as assessing the adequacy of the corrective action. At times, there even seems to be a disconnect between what the narrative describes

happened and the chosen cause from a drop-down menu. There's a drop-down menu for cause. There's a drop-down menu for corrective actions. And sometimes there seems to be a disconnect between those two.

Next slide.

Sometimes NMED doesn't have information from inspections that have happened. Just to quantify some of these issues, we reviewed a year's worth of material, and we found 23 percent of the time for medical events during that fiscal year, either there was no cause listed in NMED or no corrective action. And another 11 percent of the time, the entry in NMED was incomplete, or another 11 percent pending additional information, but quite a bit of time had already elapsed.

And a final issue which is probably not surmountable in our estimation at this point directly is that NMED really is limited. Only a limited number of people can use it. So, although we did discuss whether that was appropriate, and we decided it is, we don't have any specific recommendations extending to that, other than our Committee and the NRC promulgating findings to the community through information notices and the like.

Next slide.

Okay, so what are the requirements? What do the regulations say? So, starting off, everybody involved in medical events knows this, but you have to report, once you know about the event, within 24 hours you've got to report it. Okay? And there are some basic elements you have to include in that. That's pretty basic. So, there's an urgency to it. And it's useful in some ways, but it's a pretty limited report.

And then, the next thing is that a written report with the elements that are detailed -- and we'll show you on the next slide what those elements are -- has to be submitted within 15 days. Okay. That's really all the requirements in 10 CFR 35.3045.

Okay. Next slide.

Okay. Now the specific elements required in the 15-day report are here: licensee name; name of the physician who prescribed; a, quote/unquote, "brief description of the event"; why the event occurred; the effect, if any, on the individuals, and what actions have taken place or could have prevented a recurrence.

So, that's really the core of what's asked. Totally reasonable, but if you think about it a little bit, you will see that it's pretty vague. And although many reports can follow the letters of this requirement,

many of them really don't provide enough information to really have an idea of what's going on. So, they are following the letter of the law perhaps, but still not really achieving the initial goal that we outlined on the first slide of being able to really learn from these events.

Next slide.

Now there's a guidance document, SA-300, which really is for the Agreement States, how they are to carry out the whole process of reporting. But it's also, as I understand it, what the NRC itself uses as well. And there's some additional details in this that I'll share with you now.

Next slide.

Okay. So, in this document, the following requirements or suggestions are: follow-up information on an event should be provided. It should provide the results of the investigation as to what happened; where it happened; when it happened; how it happened, and what conditions occurred. And on a monthly basis, a follow-up report should be sent to those who have not completed the report. And that's really about it. So, there are positive suggestions, but not actual regulatory language of required, not any final deadlines of, okay, it has to be done by this

time, or whatever.

Okay. Next slide.

Okay. And the minimum elements for a complete report, according to this guidance, are listed here, pretty similar and pretty reasonable, but, again, a little bit vague. Narrative event describing everything should be happening; making sure that the patient has been informed of the event; also, that the referring has been informed, which to me is an irritant, but that's a conversation for another day. And the basic cause and corrective action things, et cetera.

Next slide.

Okay. So, the summary of our review of the actual requirements is we identified some gaps. So, the minimal requirements, the data elements, as I alluded to, seem a bit vague and, also, it's rather limited scope. There's actual no formal, official requirement that an NMED report be completed. And if it is incomplete, there is one automatic email that goes out 57 days later, and that's the end. No other outreach is done.

The final regulatory thing is, when the program is reviewed. So, the state, for example, has reviewed, and in their four-year cycle, attention is paid to how well they are regulating and how well they

are collecting the reports, as are a bunch of other things. And that's really the teeth, if you will, of the oversight.

And that would be totally great if the system was working well, but we think there are some ways to improve on the system, not necessarily by closing these regulatory gaps for now, but with some other approaches in the meantime.

Next slide.

So, we have some specific requirements that do not involve changing of any regulations, as I alluded to before. And we recommend that these be implemented, and then, we would recommend observing for a few years, seeing if they are having an impact before considering more regulatory approaches.

So, specifically within NMED, we ask that, both for the root cause and for the corrective action, which are really the key elements, that there be a narrative section that is searchable within NMED. So that information could be put in there with a lot of detail and be able to be searchable. We have actually met with, on one of our calls, with an NMED representative who assured us this could be done.

We recommend that this Committee, perhaps the Subcommittee -- we'll have to see -- develop some

materials to share with the regulated communities and the user communities about what it means to do a good NMED report. In more detail, describe what a good NMED report is, perhaps give an example of a high quality NMED report, maybe make one up or use one that is very good in the system and just redact all the potentially identifying information.

Next slide.

Okay. So, what would these elements in an educational effort to the user communities and the regulatory communities? And part of this is also educating people like why, why bother. People may not be aware that this Committee exists or this Committee actually reviews events and tries to advise people, and the more you share with us, the more we can help prevent events in the future. So, we do feel that there is a gap in that understanding, and that many in the user community would be much more forthcoming if they understood there was some good to come out of that, and not just some regulatory burden.

So, we want to ask that the community give us more detail of what happened and that we describe what's required or what to ask for in enough detail that someone who is uninvolved in the event, either an AU or a regulator who is uninvolved, could read the

event and understand what happened. And we want to know very specifically where in the process of radiation delivery did the event occur; who was present at the time; what led up to the event, and how did the event happen; who caught the event, and in what way did they catch the event, and right, how was it caught.

Next slide.

And we would like to advise that people, when they're writing their corrective action, that they talk about that narrative also being useful; what short-term and long-term corrective actions did they do, and have them articulate how the corrective action linked to the medical event. Because, as we alluded to before, a lot of times there seems to be a disconnect.

And it might just be hard to understand the whole event, because, as we described, reinforce to the users through this educational effort that any information about the manufacturer, the device, should be shared. There is a way of doing that within NMED, but it's not uniformly done. Like reports could be uploaded, for example.

We want to remind users of the medical aspects. Some of these events, while technical, intersect with medical issues. And sharing that medical aspect can be really useful for the other

Authorized Users in really kind of understanding what happened; for example, some anatomic variance that a patient might have. So, that's not an NRC -- and the regulator is not going to think about that, but for an Authorized User, like, oh, now I understand, when I have a patient who has Condition X, I really need to be thinking about this. So, you need to tell us that the patient had Condition X, so that we can kind of share that information, as an example.

Right. And the importance of including their 15-day report in what they submit. And also, ask -- we can't officially require, but ask -- and that it's really important that this whole thing be completed within a 12-month process. So, that seems like quite generous, but, within that, we can actually, at the end of the year, have a good amount of information.

Next slide.

How are we going to spread this information or how do we recommend that we spread this information? No. 1, our Subcommittee asks that the NRC put together an information notice and issue an information notice with these guidelines in there to the community.

We also recommend presentations be made to the OAS, the CRCPD, and the medical professional societies with this content.

Next slide.

So, we feel there are significant opportunities to enhance the current system by promulgating how it can be used and what really are the core elements to make a useful report. We do, however, feel that, if in a few years after successfully sharing this advice there's not been an improvement in the quality of NMED reporting, then closing some of the regulatory gaps I shared earlier might be necessary.

Next slide.

I think that concludes the report. I'm happy to take any questions.

CHAIRMAN PALESTRO: All right. Thank you very much, Dr. Ennis, for an excellent, comprehensive report.

Comments from the other members of the Subcommittee?

(No response.)

Comments from members of the ACMUI?

Mr. Ouhib?

MEMBER OUHIB: Yes, I think, on the conclusion, I just want to make a statement here. It's not only improving the quality of NMED reporting, but also help with the hope that perhaps having adequate

information, that would most likely reduce the number of medical events, because then people, like you were saying, the case he was talking about, people understand how things happen. And therefore, when they understand that, they will be prepared to look out for these kinds of situations and all that and, eventually, avoid these type of errors.

CHAIRMAN PALESTRO: Any other comments?

Dr. Schleipman?

MEMBER SCHLEIPMAN: I think it's a great report, but something to the recommendations. Just from a logistical perspective, if these are entered electronically, and we're missing 23 percent -- they are incomplete of corrective action or cause -- could there be a forced entry that you have to have this before you proceed to the next page, or whatever? So that you could not submit an incomplete report. Or are these done just by uploading documents of written reports? I'm not sure how it's actually input.

MEMBER SHOBER: So, I can speak to that a little bit. This is Megan Shober.

One of the things about medical events is that a lot of times the information kind of comes in over time. And so, a lot of times, like when you first get that 24-hour report, there's not a lot necessarily

that's known about it.

MEMBER SCHLEIPMAN: I see.

MEMBER SHOBER: Once we report that to the NRC, NMED creates a record for that. So, the initial record comes in just with the 24-hour information. And so, then, information may trickle in over a while.

So, I'm not sure that it would really work to have that --

MEMBER SCHLEIPMAN: The investigation needs to be done.

MEMBER SHOBER: Right, right.

And then, can you remind me what the second part of your question was then?

MEMBER SCHLEIPMAN: It was just that, if you're missing that many corrective actions, why could there not be a threshold where that has to be put in? People can consider this is signed off or submitted.

MEMBER SHOBER: Right. Yes. So, I am hopeful that having that as a narrative will help with that. Because, honestly, the way the pick list is constructed, almost every single event said, "Procedure modified; personnel received additional training". And that's just what, for medical events, that was conducive in the pick list.

MEMBER SCHLEIPMAN: It's not meaningful.

MEMBER SHOBER: It's not meaningful because that applies to everything, no matter what. So, I am hopeful that, with the addition of the narrative, that that will provide some of that extra detail that would be more helpful for the ACMUI kind of review.

MEMBER SCHLEIPMAN: Thank you.

CHAIRMAN PALESTRO: Other comments or questions from the ACMUI?

MEMBER GREEN: Dr. Ennis, nuclear medicine is a modality of contrast. We're always looking at the contralateral side and imaging and comparing this to that. I think it would be very insightful if we not just made a good example, but started with the current example, and then, flesh it out to what it should be. And let the leaders see the contralateral sides. Let them see what we're getting today, how it's meaningless, and then, if it was fleshed out, how you guys can learn from it.

MEMBER ENNIS: That's a nice idea.

CHAIRMAN PALESTRO: Any other comments or questions from the ACMUI?

Mr. Sheetz?

MEMBER SHEETZ: Yes, excellent report.

This is probably a question for the NRC,

but aren't almost all medical events followed up with the reactive inspection? I mean, whether it's the NRC or an Agreement State? And then, wouldn't it be possible for that, at the conclusion of the reactive inspection, to assure that all the appropriate information has been entered into NMED, so that it is a complete and understandable report?

MEMBER ENNIS: Sure.

MR. EINBERG: Yes, this is Chris Einberg.

Yes, you are correct, most medical events are followed by a reactive inspection. The other way we follow up on these NMED reports is that we have staff who tracks the reports, and if there's a gap, they periodically reach out to the Agreement States or to the licensees to make sure that the information is input into it.

Now, granted -- and this was very useful to see that -- it's not always happening. So, the NRC staff needs to do a better job following up with reaching out to the Agreement States to make sure that the information is correctly inputted or collected.

Lisa, did you have something that you wanted to add?

MS. DIMMICK: Yes. As far as reactive inspections, not all Agreement States do reactive

inspections. So, just keep that in mind. So, not all events result with a reactive inspection.

And then, a lot of the inspection data that might further document corrective actions on the part of the licensee for both the NRC and the Agreement States reside in the inspection reports. So, I think with the Subcommittee's report trying to show how going back to add that information to NMED will help make it a more complete record for people to use as a learning tool or to learn from events, is what the Subcommittee was looking at with its recommendations and providing a good example of a complete record in NMED.

CHAIRMAN PALESTRO: Dr. Jadvar?

DR. JADVAR: I just have a question. So, assuming that these reports become comprehensive and accurate and wonderful, is there plans or are there plans right now that analyze these NMEDs stratified by various procedures, locations, type of settings, to understand what type of NMEDs are occurring more, why? It kind of gets really to the bottom of this. And then, perhaps that can be just like running a clinical trial of research, kind of analyze it, and provide that information as educational material, kind of as a preventive measure to everybody, just to understand these are the things that we have analyzed.

Just not reporting and having it stored in a computer, but actually using that data for some good.

MEMBER ENNIS: Right. So, the answer is yes. My Committee that I presented on just before the break, that's its role. It's a standing committee and that's what we have done, and we will continue to do. Donna-Beth as well does a report. I think she wants to make a comment on that as well.

DR. JADVAR: Thank you.

DR. HOWE: If you look at the reports that I put out in the spring, you will see that I include a section called references. And in the references, if there is an inspection report, it will be listed there. And so, if you want to look at the inspection report, you can ask the staff to try to get that inspection report for you. It may or may not be more informative than what you are already seeing, because there is a difference in quality in inspection reports.

CHAIRMAN PALESTRO: Mr. Einberg?

MR. EINBERG: And I would point out also that we do an annual NMED report that is put out. And that kind of collects all of the information and looks at trends and does trends analysis.

We also, as part of our annual Agency Action Review Meeting, we look at various trends. If there

is a special study that is needed, we oftentimes look at, you know, do a deeper dive on the various modalities. This year, we looked at training and experience to see if any of the medical events are caused by a lack of training and experience, and it was inconclusive. But we do special studies and we do use the data to do a deeper dive in trying to do analysis.

CHAIRMAN PALESTRO: Mr. Ouhib?

MEMBER OUHIB: Yes, just to comment regarding some sort of analysis and all that. I think it's a great idea. My concern is that waiting a year for something to alert people that, hey, here's what we've found out, or whatever, that might be too -- I mean, I'd like to see something sort of like live, continuously updated that people can access within the NRC website, then say, "Whoa, look what they're seeing on the strontium-90. Here's what's going on," or whatever. That would be desirable, and I know that's probably too much to ask, but that would be my hope.

CHAIRMAN PALESTRO: Any other comments?

Mr. Green?

MEMBER GREEN: Looking backwards and looking forwards, we had a discussion about T&E and how there may be teams involved, and there may be other methods of T&E training.

Ron, on slide 9, you have the current list of data elements required in the current report. Is there any value in modifying that to include members of the team that were involved? So, was a physicist involved? Was a nuclear medicine technologist involved? What is the training of this Authorized User? Because, right now, it's just all -- I'll speak Southern -- "all y'all." Okay? It's everybody. But we have the ability to get granular data. I mean, we need that.

MEMBER ENNIS: Yes, that's good. If you go ahead a couple of slides to where we were recommending what be done?

MEMBER GREEN: Right.

MEMBER ENNIS: Keep going. Keep going. Keep going. Keep going. There we go. Okay.

So, who was present is in our list. But, getting more granular even, asking what their training and background were could be done. Obviously, we need some more work to create whatever we're proposing, and we haven't created it yet. But that's a good thought.

MEMBER OUHIB: Right, and who detected the medical event also. Is it a physicist, a physician, a nurse, whatever?

CHAIRMAN PALESTRO: Any other comments or

questions from the ACMUI? Yes?

MR. HOLAHAN: Yes. Good morning. Vince Holahan. I'm from NMSS.

Just a point that I thought I might bring up to clarify here for some of the newer members. This database is also used by academic and industrial users. Ninety percent of the events that will go on here may be something like a Troxler density gauge being run over by a bulldozer. A source used for a radiography event that doesn't completely retract, these are going to be, depending on the situation, either 4-hour or 24-hour reports, and then, a 30-day report is required after that.

And when we ask for folks to report this information, we have to get clearance from the Office of Management and Budget, OMB, to justify what type of information is reported, the amount of time that we expect the licensee to put in there, and the dollars that are associated with that. So, it's much broader than just the medical applications.

One of the things that we're most interested in, the loss of sources, Category 1, Category 2, Category 3 sources. If those things are lost, when are they recovered? So that we can go back and, then, justify to Congress, no, our regulations are adequate;

we've never lost a Category 1 source. If we lost a Category 2 source, within a matter of days it was degraded to a Category 3. What did the licensee do? Well, sometimes the sources. If they're on an oil and gas platform or lost overboard, and they're in 500 feet of water, well, no, they don't go back and try to recover them. And we try to capture that information.

So, again, I just wanted you to understand that this database, the nuclear material event database, is much broader than just these applications here.

Thank you.

CHAIRMAN PALESTRO: Mr. Einberg?

MR. EINBERG: Yes, if we could go to slide 9? It lists the requirements in 35.3045, what information needs to be collected. And then, that's codified in the rule there. So, if we were to request additional information, that would require a rulemaking. So, I just wanted to make the Committee or Subcommittee aware of that.

However, having said that, if we recommend doing training to the various communities, we can ask that they be a little bit more elaborate in the descriptions. But to actually require something would

require rulemaking.

MEMBER ENNIS: Yes. So, I think we understood that. And our approach right now, what we're recommending, is not a regulatory one, but an educational one. But could we, in the form of education, say, "This is what an ideal -- what we would like to get," even if it goes over and above these specifics? Is that --

MR. EINBERG: Yes.

MEMBER ENNIS: Yes, in an information notice or in meetings to the --

MR. EINBERG: So, the NMED contractor does annual training, and we can discuss it with them to give examples of good NMED reports and examples of poor NMED reports. And then, perhaps like you recommend, getting it on the agenda for the Organization of Agreement States and the annual meeting as well.

CHAIRMAN PALESTRO: Mr. Ouhib?

MEMBER OUHIB: I think the items that are listed in there, if you look at Item 3 first, when I look at the brief description of the event that's understood what we're looking for. We're looking from prior to where we have met a curve and so on.

And then when you look at the what actions, if any, have been taken, I mean that's, that's in the

recommendation. But we just want more details, very specific really.

And maybe, maybe a description of, the brief description ought to be somewhere. What is it? What is the brief description? What is required in the brief description, and so on.

Item 6 where we talk about actions, what are we looking for exactly, and so on and so forth.

So, maybe that's what's lacking, more details of what is expected.

CHAIRMAN PALESTRO: Any other comments from anybody here in the room? Mr. Sheetz.

MEMBER SHEETZ: So, I have a question. I see that this is what's required by regulation for the licensee to report in the event of medical events. Want to go back to the reactive inspection.

Does the regulator during the reactive inspection allow for additional information that is not contained in this regulation?

MR. EINBERG: Absolutely.

MEMBER SHEETZ: They are. Okay.

So, they would be able to give them additional information to supplement.

MR. EINBERG: Right.

CHAIRMAN PALESTRO: Any other comments or

questions? Ms. Shober.

MEMBER SHOBER: Yea. Mike, just a follow-up on your comment, too. There's a -- NRC has an inspection procedure for how to do a reactive inspection following a medical event. And it's pretty detailed as far as the information that should be collected. And, so, I mean this is the starting point, and then any inspection that's done is going to be -- the inspector is going to want an exhaustive story.

MEMBER SHEETZ: That is what I assume.

MEMBER SHOBER: Yeah.

CHAIRMAN PALESTRO: Any other comments or questions? Comments? Dr. Metter.

VICE CHAIR METTER: On these medical events, I still am unclear as far as the reason why they were incomplete. Could the information get gleaned from the reactive inspection report?

MEMBER SHOBER: This is Megan Shober again.

So, one thing to clarify is that the inspection reports are only referenced with the NR -- events that happen in the NRC states because they are included in ADAMS.

So, at the present time, agreement states are not providing the inspection report. There's no,

like, mechanism to do that. So that's something that we talked about in our subcommittee. And there's some possibilities or ways that that could be encouraged. And I think NRC is open to including some of that information in ADAMS.

But, regardless, as the subcommittee is doing it's work, if you have questions about an event that happened in an agreement state, we can ask the agreement state for the inspection report. That's not a -- that's a barrier that is easy to overcome.

So, we should, we should be cognizant that that is an option and not just be stuck with, oh, this doesn't provide enough information.

CHAIRMAN PALESTRO: Dr. Ennis.

MEMBER ENNIS: Just to kind of connect the dots between different subcommittee efforts we've had in the last couple years, we had an effort trying to move NRC away from reactive inspections that many of us felt create a punitive versus a -- punitive culture as opposed to a more modern safety culture.

But, I would not really want this to go in a direction, okay, we're going to rely on reactive inspection reports to help us do this job because we are really then kind of working across currents. And our encouragement here to educate people prior to that

is because you can learn something, and we can all learn something, which I'd rather us move the community towards wanting to report and not relying on a reactive inspection report.

So, that being said, of course, if done, the information might be useful. But I wouldn't want us to be taking a position that, okay, if we really want a reactive inspection every time so we can get the kind of information that we want, that is not a solution to the problem, that's taking a step backwards.

MEMBER SHOBER: And this is Megan.

Again, just another point to consider is that reactive inspections are I would say pretty close to universal when it comes to overdoses. But when it comes to underdoses I think there's more latitude to gather your information in different ways.

So, I don't know if that trickles down in the report, too, the ones we're finding are lacking information I would guess probably are the ones that are underdoses. I don't know if that's true.

MEMBER ENNIS: Yeah. No, I don't think, I don't think any of us actually --

MEMBER SHOBER: Because I know that attention goes to when there's an overexposure.

MEMBER ENNIS: Uh-huh, right. Although

an underexposure is equally, from a patient perspective can be equally problematic.

MEMBER SCHLEIPMAN: Right.

CHAIRMAN PALESTRO: Any other comments or questions?

(No response.)

CHAIRMAN PALESTRO: Comments or questions from the bridgeline?

MR. EINBERG: If you could just wait a moment, I got some feedback and it takes a little while for them to open it up.

(Pause.)

CHAIRMAN PALESTRO: All right. Hearing none, can we have a motion to accept the report of the subcommittee?

MEMBER SHEETZ: So moved.

MEMBER WOLKOV: Second.

CHAIRMAN PALESTRO: Dr. Wolkov second. Mr. Sheetz.

Any further discussion?

(No response.)

CHAIRMAN PALESTRO: All in favor.

Any opposed?

Accepted unanimously, without change.

MR. EINBERG: So, Dr. Palestro.

CHAIRMAN PALESTRO: Yes?

MR. EINBERG: There was two recommendations in the report. Should we track those as open items? And the first one is the internet program should have a narrative field, root cause, and correction action sections in additions to the existing pick lists.

And the new narrative field should be a searchable pretext section.

At a subcommittee meeting, representatives assured the subcommittee that this can be done and it's the first subcommittee recommendation or committee recommendation now.

And then the second one is that NRC, in coordination with the ACMUI, should provide additional information to NMED users and best practices for writing NMED reports for medical events.

So, those are the two open items, or action items that we should be tracking?

CHAIRMAN PALESTRO: Yes.

MR. EINBERG: Thank you. We'll take care of that.

CHAIRMAN PALESTRO: All right. The next topic is a presentation from the Subcommittee for the Evaluation of Extravasations. Melissa Martin is the subcommittee chair. She's not able to attend this

meeting, and it will be presented by Mr. Richard Green.

MEMBER GREEN: Thank you, Dr. Palestro.

Ms. Martin knew she could not be in attendance at today's meeting, and perhaps has misplaced faith, but she's asked me to present in her absence.

(Laughter.)

MEMBER GREEN: First of all, next slide please.

No members of the subcommittee have any disclosures to report.

Next slide, please.

This is the membership of the committee: Dr. Dilsizian, Ms. Martin, Mr. Sheetz, Ms. Shober, and Ms. Weil, with assistance from staff, Maryann Ayoade and Said Daibes.

We can start with the next slide and looking at what our charge was. Our charge was to reevaluate a decision made on infiltrations and extravasations that was done in 1980. And then once we reevaluate that, provide recommendations going forward: should it stay the same, should we revise that?

Next slide, please.

This all came about in the spring meeting in April where the subcommittee was established and

commissioned by Chair Palestro. And so, we set about to do that task.

Next slide, please.

Starting off, we had to get historical. What was the criteria for misadministration back in 1980 when this decision was made?

Misadministration means the administration of the wrong source, perhaps to the wrong patient, through a route of administration that was unintended, or a diagnostic dose that differed by more than 50 percent from the prescribed activity, or a therapeutic dose prescribed -- differing by more than 10 percent from the prescribed activity.

Next slide, please.

And at that time we, the request -- this has been, this is not the sole time that the NRC has discussed this topic of extravasations. It came up in also other times.

So, there was a specific request for the NRC to review this that came in May of 1980. And the definitions of extravasation is the infiltration of the injected fluid into the tissue surrounding a vein or artery. If a needle slips or, you know, some of the dose is dropped in antecubital but not into the vein, the venous system.

Extravasation frequently occurs in otherwise normal intravenous or intra-arterial injections. It's a fairly common occurrence that cannot be predicted.

It's virtually impossible to avoid. And, therefore, the Commission does not consider extravasation to be a misadministration.

And that was the request that we were asked to review that came from May of 1980.

Next slide, please.

Well, terminology has changed since 1980. 10 CFR 35.3045 now defines the term as medical event as opposed to misadministration. That changed in 2002.

And the definition for medical event is defined now to be a total dosage of more than 20 percent difference from that delivered dose.

Next slide, please.

So, I said that this has come up more than once in the course of history. In addition to the 1980 decision, clinical aspects of extravasation was discussed previously by ACMUI on two different occasions, in December of 2008 and May of 2009 meetings. Both of those meetings did not change the current feeling on that decision that was made in 1980. So, both decisions of these meetings did not have any

material effect in the definition made.

Next slide, please.

So, fast forward to spring of this year where a presentation was made describing a technology that would allow a clinician to detect an extravasation of a PET radiopharmaceutical injection by using a series of probes on the injection arm and a contralateral arm. And we saw several communications and letters from practitioners and clinicians that described how this might change patient care and the care of a patient. So, it has a value, a potential to change the standardized uptake value, or SUV, as calculated in positron emission tomography procedures.

Next slide, please.

We have to realize that extravasation is a very, very small occurrence. We have millions of injections of radiopharmaceuticals per year to millions of patients of all radiopharmaceuticals. While extravasation does not occur only with certain classes, if it's intravenous or even intrathecal, if it's injected you can have loss of materials outside the intended space. It's not limited to just positron emission tomography drugs.

The prevention of extravasation is more a matter of practice of medicine and a training issue

for medical care providers, whether that be physicians or individuals working underneath their direction, the nuclear medicine technologist.

Next slide, please.

Currently there are 48 FDA approved radiopharmaceuticals currently in the marketplace, including five which are intravenous therapeutic radiopharmaceuticals.

The material that was presented at the spring meeting was a technology that could detect extravasation of one of the six fluorinated PET drugs: sodium fluoride, FDG, fluciclovine, or any of the three beta amyloids. They're all F 18 label drugs.

It was noted during our discussion that the SUVs are not solely relied on when making a medical diagnosis. It's a contributing factor that goes into the mix but is not solely relied upon.

Next slide, please.

For isotopes other than FDG, it's difficult to quantify. If we were to make extravasation a medical event, then there would have to be an attempt made to quantify the amount of radiation exposure from the portion of the radioactive drug that was not injected intravenously successfully. Some was, some was not. How much was not? What was the radiation dose from

that portion?

Many radiopharmaceuticals will, if not injected intravenously successfully, but are deeper in the antecubital, for example, will eventually make their way into the circulatory system, which is not a problem for many radiopharmaceutical procedures such as a bone scan with a 3-hour delay post-administration.

To our knowledge, total doses in these extravasations meet the NRC's medical event criteria. The event criteria is an "and" statement, not an "or" statement.

Next slide, please.

So, the committee does not consider extravasation to be a de facto medical event. Extravasation can occur in an otherwise normal intravenous or intra-arterial injection. And it cannot be predicted. I think it's possible to avoid it. I think with training and experience practitioners can get better but you can't predict when extravasation will occur.

Not all nuclear medicine cameras have the capability to quantify the amount of radiopharmaceuticals that did not successfully get injected into the vein, so it's very difficult to quantify the amount of blood that's not in the

circulatory system. And the subcommittee members were unaware of any cases of documented patient harm that resulted due to extravasation as of today.

Next slide, please.

So, the subcommittee's recommendation was to reaffirm that extravasation is a practice of medicine issue and is not an item that needs to be regulated by the U.S. NRC.

Next slide, please.

There is no evidence at this time for the subcommittee to recommend a reclassification of extravasation at the injection site for radiopharmaceuticals to be considered a medical event.

And the subcommittee recommends extravasations that lead to unintended permanent function damage be reportable as a medical event under 10 CFR 30.3045(b) as is currently in the regulations.

Next slide, please.

The subcommittee recommends that extravasations be considered a type of a passive patient intervention, similar to the recommendations from the ACMUI committee presented in October of 2015, referenced in the Patient Intervention Subcommittee Report, dated April 2017. And should be captured in NRC's current definition of patient intervention under

10 CFR 35.2.

There was one minority opinion.

Next slide, please.

One member of the subcommittee had a different perspective on potential medical event reporting due to extravasation. This member wanted extravasation occurrences that trigger a medical event criteria of greater than 50 rem tissue dose or greater than 80 percent of the prescribed dose delivered to the patient to be reported as a medical event. This would be consistent with all other medical events that cause no patient harm, and are currently required to be reported.

The exclusion of extravasation is inconsistent with other regulations and is unwarranted.

That concludes the report. Dr. Palestro.

CHAIRMAN PALESTRO: Thank you, Mr. Green.

Comments from other members of the subcommittee?

(No response.)

CHAIRMAN PALESTRO: Comments, questions from the ACMUI? Mr. Ouhib.

MEMBER OUHIB: I have a question.

I guess my question would be, so if I remember correctly, one of the slides you recommended

that would go under patient intervention. Is that correct? So that data will be available, this sort of data will be available.

I guess what I'm trying to get to is that how are the authorized users going to learn about these episodes and be prepared or perhaps avoid it if possible?

MEMBER GREEN: I think they can be avoided by, you know, perhaps the utility for tools such as were introduced to us at the spring meeting is in a training program for nuclear medicine technologists.

Looking at patient X presenting to prepare and receive this nuclear medicine procedure, you can't predict whether an extravasation will occur.

Just like when you do an interior arterial brachytherapy with yttrium spheres, there are anatomies you don't predict, and occlusions, and pressures. And that's been marked down as patient anatomy. And so --

MEMBER OUHIB: As of now. With the technology evolving we might for a couple.

CHAIRMAN PALESTRO: Dr. Dilsizian.

DR. DILSIZIAN: It's very important to make sure that we don't, NRC doesn't overreach and get into medical care. Access IV, phlebotomy, we all get blood drawn, we get some hematoma there as part of the

procedure. Go to the veins, there sometimes will be some trauma. It's part of the procedure of medical care.

Can you be trained to be better? Absolutely.

Should all technologists, physicians do their best not to have extravasation? Absolutely.

Does that mean that it's not going to happen? It will.

The other part is that if you can't quantify something, you can't regulate. We can't quantify this, so therefore we can't regulate. I think that those two are the key points here that will move the extravasation issue along.

MEMBER OUHIB: I think what I'm trying to get to is that information sharing, would that be left to a professional organization to, to sort of tackle that or?

DR. DILSIZIAN: Well, I mean, when you say information, that's the key. I mean, it's global. You're saying, well, what is the information? You don't have the information.

The information is that extravasations occur. That's the information we all know. What data are you going to be providing that's reliable and

quantifiable that we're going to learn from?

What you're going to learn from is do your job right, try not to have a lot of extravasation. That's medical care. Nothing to do with dose. Any, phlebotomy or cath, anybody accesses a vein or artery should be careful not to do that. That's medical care.

MEMBER OUHIB: This long-term, short-term effect, would that be good information?

DR. DILSIZIAN: Well, give me an example. I mean, there's -- remember, millions of procedures are being done annually, daily. Do you know of any procedure that? Okay, no, I'm just saying, we don't.

MEMBER OUHIB: We don't.

DR. DILSIZIAN: I mean, if we do, that would be great. We don't.

CHAIRMAN PALESTRO: Mr. Sheetz.

MEMBER SHEETZ: The subcommittee was consistent with the prior determinations of it should not be, extravasation should not be considered a medical event. If it was considered, then it would be the burden of the licensee to evaluate every radiopharmaceutical administration and determine the plus or minus 20 percent extravasate, and what was the flow, did it exceed 50 rem to the tissue?

That is, first, it would be impractical

to for every radiopharmaceutical administration.

And so, we were consistent with it's a practice of medicine. It happens with no error on the part of the person administering the vein care, or that can be similar.

Where we did change is that we said for those extravasations that we saw in permanent functional variants -- and I think that's really the first one we want to capture is was there some patient harm, that would be reportable. And the way that would be reportable is if we consider extravasation for infiltration to be captured in the patient intervention regulation. Currently it is not. But if we could include that in the definition of patient intervention, then we will capture those events that result in patient harm.

Thank you.

CHAIRMAN PALESTRO: Other comments or questions? Dr. Schleipman?

MEMBER SCHLEIPMAN: Just to say following up on Dr. Dilsizian's point is that healthcare institutions don't need the force of the NRC regulation to determine their extravasation rate. The Society of Nuclear Medicine published a, don't know how long ago, a quality assurance manual that had an option for,

and we actually applied this to monitor extravasation. Not to calculate, quantify the dose but to determine the rates, to develop training to improve the education.

So, this is all available in the current milieu of quality improvement, and so forth. And that the regulations don't really need to be changed to have people doing the right thing so to speak.

CHAIRMAN PALESTRO: Other comments or questions? Yes?

MR. LATTANZE: This is Ron Lattanze. I spoke earlier, last April. Nice to see everybody again.

Mr. Green, you did a nice job filling in for Ms. Martin.

I wanted to talk about a couple of points that I've heard today. And I'd like to start with the fact that the subcommittee, thanks for considering the request to begin with. And it appears that the subcommittee has come back with that there may not be any patient harm as a result of extravasations. And you're talking about permanent functional damage, I believe was the term.

And there was also a comment that there's a belief that it's not actually, you know, that it's considered medical practice. And so I just have a

slightly different view on this matter.

And I think the question is -- and it was brought up in Slide 18 which was the minority opinion, which is when you have an extravasation you leave dose behind in the tissue. And it is possible to actually estimate or quantify now what the dose that's left in the tissue is. And it can exceed the NRC's reporting limits, and often does.

Now, I'm not saying that every extravasation should be considered a medical event. I'm not saying that at all. But it is happening frequently enough, and the severity of some of them are happening to the point that you can actually very -- fairly accurately estimate how much dose was left behind and be able to provide to the NRC that perhaps, as we did in two examples since I met here in April of last year, to the subcommittee I provided two examples of severe infiltrations that resulted in doses that exceeded, dramatically exceeded the NRC reporting requirement.

And the question is, if that happens, if you know that you have a dose that exceeds the NRC reporting requirements -- and going on Mr. Ennis, Dr. Ennis' previous presentation about adherence to reporting requirements, and what the purpose of

reporting requirements are -- these should be reported.

And it doesn't matter whether it happened so, on April 14th of 2018, the NRC received a medical event report on a case, I think out of North Dakota, where somebody spilled 15 millicuries on the patient. And it qualified as a medical event.

So, you can spill FDG on a patient which you can then wipe up after you, after you know they've been exposed. And that's required a medical event. But you can dump 15 -- you can spill 15 millicuries of radio tracer into a patient's tissue and let it sit in the tissue, mostly unknowingly, oftentimes unknowingly, and not have that as a reportable event, which is completely inconsistent with what, I think what we're trying to do here to protect patients.

And so a couple other thoughts I have is I just want to make sure the entire ACMUI understands I presented back in April, in 21 minutes of prepared comments. Since that time, as Mr. Green mentioned, we've provided more information to the subcommittee, including two case reports that I just described that exceeded the limits. Also, a published paper that was published and had a print in the Journal of Nuclear Medicine Technology that describes that infiltrations can in fact be dramatically reduced if they're

monitored.

And somebody mentioned earlier that this is available now today. Quality improvement processes exist. Yet, the rate today of infiltrations in nuclear medicine is very consistent with the rate probably back in 1980, 1995, and 2002. It's around, we think, 15 percent, based on our observations. And it hasn't changed, despite having -- despite, you know, quality assurance plans being put in place.

And so, while I don't consider -- while I don't think any of us should consider that the training of people and how they should do injections should be regulated by the NRC, I do believe that when an improper administration of the radiopharmaceutical happens that exposes patients to over the limit of the NRC reporting requirements, that should be reported as a medical event.

And so, those are the main points. And happy to answer any questions, any disagreement.

CHAIRMAN PALESTRO: Dr. Ennis.

MEMBER ENNIS: Just as a point, that I think the technology is only there for FDG.

MR. LATTANZE: Oh yeah, thank you. Thank you for mentioning that.

No, the technology is not just for FDG,

it can be used in any radio tracer and also any radiotherapeutic. It has different energy levels, so the sensors can be changed to accommodate all radioisotopes.

And that reminds me, there was a comment that there were none -- I think it said there was no evidence of any of these other radiopharmaceuticals ever being a reportable event. We'll be submitting two MDP Technetium bone scan cases where we estimate that the actual radio tracer provided something way in excess of the reportable dose requirements by the NRC. Later this month we'll be submitting those.

And what we found is, some of you also mentioned the biodistribution, right, so when you inject a straight stick of MDP into a patient's arm for a bone scan and it's not flushed, and you dump the entire dose of 27 millicuries into the patient's arm with a half-life of 6 hours of the Technetium, that does actually exceed the NRC reporting limits. So, we'll be submitting those as examples.

Yes?

MEMBER ENNIS: Just another point of clarification. So, in your mind are you suggesting that, like, your idea, well, every radiopharmaceutical injection would have an assay field done to determine

whether infiltration above some threshold for that isotope occurred? Is that what you believe is necessary?

MR. LATTANZE: Yeah. So, what I would recommend is that if the NRC were to change their policy -- not the rule, the rule I think is, the medical rule is fine -- if they change their policy to exempt infiltration from being reported, that will force providers to begin figuring out some way to monitor their injections, whether that includes putting the injection site in field of view, whether that means putting a Geiger counter on that, whether that means putting a hard probe on it, it doesn't -- I'm not concerned about the process in which they'd use.

But today, and I had this conversation with the leader of SNMMI, Dr. Dilsizian, probably a week ago, their self-selection process for people who are in some of these leadership positions, they're usually the best of the best, and they're associated with the best of the best, and what they don't see is that in a mobile unit in western Virginia that 80 percent of the time patients are being infiltrated.

And more than half of those are being infiltrated in very severe amounts.

And I would strongly discourage that the

committee recommend that you include this as a passive patient intervention as a method for classifying these issues. Our experience in over 16,000 cases is that patient anatomy, patient size and BMI matters. But you can take different technologists with different techniques and they can actually do the injection in these patients very well, very consistently.

But it's not a patient issue that they're being infiltrated, it's a technical issue in the procedure itself, either in flowing the vein, accessing the vein. And so, that would be a strong recommendation to discourage that request.

CHAIRMAN PALESTRO: Ms. Shober?

MEMBER SHOBER: Yeah. My question maybe you can help me straighten this out in my mind. With a therapeutic dose you have a written directive that includes a prescribed treatment site. But for diagnostic radiopharmaceuticals there's no prescribed treatment setting.

So, when you're talking about administering this radiopharmaceutical, I'm just, I'm not convinced that an extravasation is going to meet the plus or minus 20 percent threshold for a medical event. So, it has to be both plus or minus 20 percent and the 50 rem dose to an unintended site.

And that's the part that I can't, I can't reconcile that right now. It seems like if you're administering the dose to the patient, the rule is silent about where that dose has to go. And I think that's the difference between the North Dakota case that you mentioned, that never made it inside the patient.

So, if anyone has any thoughts about that or how to reconcile that piece of it, that would be helpful to me.

CHAIRMAN PALESTRO: Dr. Howe?

DR. HOWE: Yeah, if you, if you look at the medical event requirement, reporting requirement, you'll see that the diagnostic medical event, the diagnostic procedures do not have a written directive. But, the diagnostic procedures are supposed to be good and in accordance with the licensee's procedures.

So, you have procedures that say a bone scan is so many millicuries, an MAA is so many millicuries. So, that's within the diagnostic procedures. And so that's what you use instead of a written directive for the diagnostics.

And then when you get to the therapeutic or over 30 microcuries of I-131, now you're looking at a written directive. So, we do capture the

diagnostics but it's according to the diagnostics medical procedures that the licensee has. And then they cover the others with a written directive.

So, but the other thing is, not only is it over 20 percent but it has to be over a certain dose limit. And that dose limit did not exist back in 1980. It just came into being probably in the '90s. Okay?

CHAIRMAN PALESTRO: Other comments or questions?

(No response.)

CHAIRMAN PALESTRO: Thank you.

MR. LATTANZE: Thank you very much.

CHAIRMAN PALESTRO: Comments or questions from individuals in attendance here in the room? Dr. Howe?

DR. HOWE: I just wanted to follow up on what Mr. Sheetz said. And that is, in this slide it implies that the current definition of a medical -- of patient intervention would capture this. And it does not. Because the current definition is an action taken by the patient. An extravasation is not an action taken by the patient.

So, you would need rulemaking to capture this in the patient intervention section. You could use the patient intervention thresholds if you want

to modify the medical event reporting for extravasation that would ensure that you don't have every extravasation, just the important ones.

I just wanted to make sure that's clear.

DR. DILSIZIAN: I'd like to respond to that.

CHAIRMAN PALESTRO: Dr. Dilsizian.

DR. DILSIZIAN: But, Donna, we were talking about the recent discussions we've had, and I was the chair presenting that. Remember that when we were saying when you administer TheraSpheres there can be anatomical anomalies that is passive intervention. Even though the patient didn't move, it's the way the tracer went the direction that it shouldn't have gone. And we defined that as passive intervention, not just patient motion.

We actually expanded that definition. I know it's not part of the rule in the books yet. I understand that. But that's what we were talking about. And that this committee had discussed it or presented it to you. I know it's not in the rulemaking yet, but that's how we're using the term passive intervention. We hope that it can be expanded, that it's not just patients moving, that it's anatomical variations, including venous variations that may result

in extravasation.

DR. HOWE: And that was my point. You need to have a rulemaking --

DR. DILSIZIAN: I understand.

DR. HOWE: -- to put the process into the definition for patient intervention.

We were able to do that in the TheraSpheres because in 35.1000 guidance.

CHAIRMAN PALESTRO: Mr. Sheetz?

MEMBER SHEETZ: Yeah. My intention was that it be captured in the definition --

DR. DILSIZIAN: Yes, yes.

MEMBER SHEETZ: -- of patient intervention. Now I see the difference with respect to why maybe that's in Part 1000.

So, there's no way to expand this definition to capture this particular situation.

So, may I ask then, I always give an example with Gamma Knife for patient intervention, is the patient's receiving a treatment and halfway through the treatment they go into tachycardia. And they flush the treatment and the patient has to go to the ICU. And they cannot complete the treatment, so they go over 50 percent of the dose is outside the plus or minus 20 percent.

So, I would just consider that patient intervention. Is that not true?

DR. HOWE: No. That, that would be a medical event. But we would expect the medical facility to do what is correct for the patient, which would be take them out of the Gamma Knife, treat them properly. Because a medical event is not a violation, it just happens to be a report of why the treatment was stopped. And in this case the treatment is stopped because of a patient consideration.

But that's not patient intervention because the patient didn't actively do anything. They just had a heart attack in the middle of your procedure.

CHAIRMAN PALESTRO: Any other comments or questions?

(No response.)

Comments or questions from the grid line -- bridgeline? Excuse me.

(No response.)

CHAIRMAN PALESTRO: Dr. Ennis?

MEMBER ENNIS: So, for the subcommittee and the colleagues, can we envision any kind of agent whose delivery intravenous or intra-arterial would be distinct from any other IV or IA access?

CHAIRMAN PALESTRO: I'm sorry, Dr. Ennis,

would you repeat the question?

MEMBER ENNIS: Yeah. Are any -- do we perceive any new agent or any current agent is the way it's delivered when we do intravenous, is that any different than any other intravenous or intra-arterial administration?

My thinking is if it's just the same application, same, you know, IV line as it is for anything else, that's just medical procedures and, yes, there are mistakes. But there's nothing getting at the radiation aspect. It's not a radiation safety issue. I understand the subcommittee's perspective. But there ought to be something that somehow would be radiation specific because of the administration.

And then, then in my mind I could understand the argument why we would want to regulate those or ones that meet some kind of threshold.

CHAIRMAN PALESTRO: Any other comments? Yes, sir.

MR. LATTANZE: Can I ask a clarifying question, Dr. Ennis? So, are you saying is the way that a nuclear medicine radiopharmaceutical is injected different from any other?

MEMBER ENNIS: Yeah, in some kind of substantive way where it's a unique kind of procedure,

if you will, and therefore subject to a kind of different thinking?

MR. LATTANZE: Yes. So, you know, our experience is that when technologists inject a radiopharmaceutical, even though it's through IV access, it is slightly different than, say, for example, a contrast CT agent or a chemotherapy injection. And oftentimes if they're using a straight stick, they're of course, handling a very large syringe, shielded syringe and trying to do the injection that way, which is different.

And when they are drawing a dose, a lot of times -- and I've been in, I've been in probably hundreds of cases now, they'll gain venous access with the patient and then the patient actually is sitting there for 15 minutes or so while they go draw a dose. And then they come back. And if they somehow manipulate the IV differently or the butterfly differently they can end up causing an infiltration or an extravasation that way.

So, I think there are some differences in the way that it's administered with a radiopharmaceutical compared to some of the other items.

CHAIRMAN PALESTRO: Any other comments,

questions?

(No response.)

CHAIRMAN PALESTRO: Anyone on the bridgeline, comments, questions?

(No response.)

CHAIRMAN PALESTRO: All right, hearing none, then it's time for a vote.

Do I have a motion to accept the subcommittee's report?

MEMBER SCHLEIPMAN: So moved.

CHAIRMAN PALESTRO: Mr. Schleipman.

MEMBER WOLKOV: Second.

CHAIRMAN PALESTRO: Second, Dr. Wolkov.

Any discussion?

(No response.)

CHAIRMAN PALESTRO: So, there are, I'd just like to go through this to clarify it. There are three recommendations.

And one, the first is extravasation is a practice of medicine issue and not an item that needs to be regulated by the NRC.

Is that the subcommittee's intent to say that there should be no change in the way extravasations are approved?

MEMBER GREEN: I believe that's --

CHAIRMAN PALESTRO: -- or viewed? Is that correct?

MEMBER GREEN: I believe that's the primary conclusion.

CHAIRMAN PALESTRO: Then the subcommittee recommends that extravasations be considered a type of passive patient intervention.

And as Dr. Howe pointed out, that would require a change in rulemaking. Am I correct?

Am I correct, Dr. Howe?

DR. HOWE: That's correct.

CHAIRMAN PALESTRO: And then your last recommendation is there's no evidence to recommend a reclassification at the injection site to be considered a medical event.

Mr. Einberg?

MR. EINBERG: Yeah. So, under the second recommendation where extravasation should be considered a passive patient intervention, under the current rule, as Dr. Howe pointed out, that would require rulemaking. So, I think the recommendation should be that under future rulemakings, extravasation should be considered a passive patient intervention. So, the report should be modified accordingly.

CHAIRMAN PALESTRO: That under future

rulemaking?

MR. EINBERG: Under future rulemakings, yes. Future 10 CFR Part 35 rulemakings, making revisions to CFR Part 35.

CHAIRMAN PALESTRO: So, we'd amend the second bullet to -- I just want to make sure I have this correct, Mr. Einberg.

The subcommittee recommends that under future 10 CFR Part 35 rulemaking extravasations be considered, so forth and so on. Is that correct?

MR. EINBERG: That's correct.

CHAIRMAN PALESTRO: So, then we need to modify the motion; is that correct?

MR. EINBERG: Correct.

CHAIRMAN PALESTRO: I'll ask, Dr. Schleipman, did you make the initial motion or?

MEMBER SCHLEIPMAN: Oh yes. Yes, so I would move to put a report, the amended report to be revised.

MEMBER WOLKOV: I'll second.

CHAIRMAN PALESTRO: Any further discussion?

(No response.)

CHAIRMAN PALESTRO: All in favor?

Any opposed?

The motion is passed unanimously.

Thank you. And I believe that that concludes the morning session. And we now are on break until 1:30.

(Whereupon, at 12:01 p.m., the above-entitled matter went off the record, to reconvene at 1:30 p.m.)

MR. EINBERG: All right. Welcome back everybody. It's time, I think, to reconvene the meeting.

Okay. We have a special guest today, Chairman Svinicki. And so thank you for your presence here. And to make some special remarks to Dr. Palestro.

NRC CHAIRMAN SVINICKI: Well, thank you all very much. And I appreciate this opportunity. And I'm very, very pleased to be a part of kind of interrupting today's proceedings. But for something that's, I think, on behalf of the Commission, very, very important that we recognize.

So, I am here today to provide both NRC's, but also on behalf of my Commission colleagues, I want to recognize Dr. Christopher Palestro for his myriad contributions to the Advisory Committee on the Medical Uses of Isotopes.

And the NRC staff is very helpful. So they provided a list that is so long that it would take the

remainder of the afternoon to read to you, all of the singular contributions that he has made to the ACMUI.

And in the Commission's meetings with the ACMUI I've sometimes remarked that the particular expertise represented on this particular advisory committee, we have a singular dependency on having people of such superior capability, their willingness to serve as members of this committee.

And Dr. Palestro has not only served for eight years, which is both astonishing and phenomenal, and we're very, very grateful for. He is of course, finishing up his time on the Committee as its Chairman.

And moreover, he has chaired, I believe, at least three subcommittees that had very substantial undertakings. So, it's clear just by that alone that his devotion and commitment to the work of this advisory committee has been exemplary.

And I think from that it speaks for itself. And he also, of course, has represented the very important capacity on the Committee of being the nuclear medicine physician representative. Which is something that is uniquely, has a unique nexus to the Commission's regulatory role here.

So, I know on behalf of myself and all members of the Commission, we're very, very grateful

to you. Again, I sometimes remark, thank goodness for the people of your caliber and your colleagues here who are willing to serve on this advisory committee.

The Agency's in this unique position where we have a regulatory role, but medicine is not really our central regulatory role. So, thank you to all members of the Committee.

And I'm certain I join them in our thanks and gratitude for your long service on the Committee. There are, of course, this being a federal government agency, some commemorative items that I want to provide to you.

The first is -- microphone again. The first is a U.S. flag that has been flown over the U.S. Capitol on the -- at the request of U.S. Senator Chris Van Hollen of Maryland.

So, this was flown on your behalf. And there's the certificate that commemorates that.

(Applause)

NRC CHAIRMAN SVINICKI: And there is also a certificate of appreciation and an NRC commemorative pin as well.

So, we're not loading you up with too much here.

(Laughter)

NRC CHAIRMAN SVINICKI: Thank you again.

(Off mic comments)

NRC CHAIRMAN SVINICKI: Okay. Thank you again. Just my sincere thanks and gratitude.

CHAIRMAN PALESTRO: Thank you.

(Applause)

CHAIRMAN PALESTRO: Well, the time has come. I'm trying to think about what I would like to say. I'd like to say that it's been a pleasure to have had the opportunity to serve on this committee for the past eight years.

But I don't think pleasure does just -- the word pleasure does justice to my feelings. It's been much more than a pleasure, it has been an honor to be able to serve on this committee for the past eight years.

And to be very honest with you, I'm humbled and I'm almost speechless that the Chair of the Nuclear Regulatory Commission took time out of her busy day to come down and spend a few moments and acknowledge my contributions.

And I promise you, Madam Chair, that I will be brief in my comments. I don't want to tie you up.

(Laughter)

NRC CHAIRMAN SVINICKI: You've got eight

years to reflect on.

(Laughter)

CHAIRMAN PALESTRO: I'd like to think that I've made important contributions to the Committee, to the Nuclear Regulatory Commission, to society in general over the past eight years, but I'm not the one to judge. It will be judged by others in the future.

But what I can tell you, having had the opportunity to serve on this committee, and particularly to serve as Chair for the past year and a half or two years, clearly ranks with, from a personal standpoint, among the highest achievements that I could have ever hoped to have achieved in my career.

And I thank you all for that opportunity. It shouldn't all be about me however. And I think that one of the things that I learned, or at least came to have a better understanding of over the past year and a half that I served as chair, how much work is done by, I really don't like the term, but I'm going to use it, because that's what it's referred to, is staff.

It's kind of a pedestrian term for a group of highly educated, sophisticated, professional individuals. But nevertheless, that's the designation.

But to people, Sophie Holiday, Chris Einberg, Lisa Dimmick, Donna-Beth Howe, Andrea Kock, and anybody who I might be leaving out, I apologize. Clearly, we, I personally, and we as a committee, owe you a debt of gratitude, and continuing thanks for all of the work that you do.

For example, if you look at these outlines and the booklets that are put together for these meetings. It's true that the Chair and the Vice Chair contribute suggestions and help organize it. But the bulk of the work is really done by staff.

The meetings, getting organized for the meetings. Trying to wade our way through the Concur travel.

All the times, at least I personally, all the trouble I've had trying to sort through that. Forgetting my password and having to torment Sophie, who was handling it at the time.

And the response certainly, at least via email, I don't know what they're saying to themselves, but via email, is always a smiling emoji, and they're more than happy to help me with it.

(Laughter)

CHAIRMAN PALESTRO: And after eight years, I know when I go back and try to fill out my report,

I'll have more problems and make more mistakes.

But clearly, it's a tremendous amount of work that they do. And I never really understood or appreciated it until I became Chair of the ACMUI.

And then finally, it's important that we remember not only are they interfacing with us, the ACMUI and our subcommittees, but they have to interface with management.

They have to interface with the Commission. They have to inter -- excuse me, interface with the public and all of the various stakeholders. And that is a -- to say that it's not easy would be an understatement.

And yet they do it all very well. And they do it pleasantly. And they do it with smiles. And these aren't the only responsibilities they have.

And so, as much as you are acknowledging me today, I think it's very important that we acknowledge them. And I would like to offer them, on behalf of myself and on behalf of the ACMUI, heartfelt gratitude for everything that you do.

(Applause)

CHAIRMAN PALESTRO: And in conclusion, if there was an exit interview, I would imagine that I would be asked typical questions, two questions. The

first question is, what did you like most about serving on the ACMUI?

Well, that's a very easy question to answer. Having the opportunity to interact with, to mingle with, to meet, to become friends with such an eclectic group of individuals over the past eight years.

The second question that the interview undoubtedly is going to ask, or would ask is, what did you like least about being on the ACMUI?

And that's an equally simple response. Having to say goodbye. Thank you very much.

(Applause)

(Off mic comments)

MR. EINBERG: And also, we have the Office Director, John Lubinski, who would like to make a statement.

MR. LUBINSKI: Thank you. I really appreciate your comments and your service. I've only had an opportunity to literally meet you twice and being here for only four or five months now.

But, really appreciate the eight years you've contributed. And you know, the Chairman coming down. I really appreciate her coming and doing a presentation.

But I also want to give you a thank you

letter. That we appreciate everything. It's signed by the NRC staff. And we appreciate your comments and we appreciate everything you did to support us over the years.

CHAIRMAN PALESTRO: Thank you.

MR. LUBINSKI: Thank you very much. We appreciate it. Thanks.

(Off mic comments)

(Applause)

CHAIRMAN PALESTRO: Thank you. And before we get started with the schedule that we're submitted. Is there anybody else on the committee who would like to make a statement?

Yes, Dr. Metter?

VICE CHAIR METTER: Dr. Palestro, I'd like to thank you for your guidance. When I first started on this committee in 2016, for all your help.

And just to learn about the workings that we do. And you've really been a great mentor. And thank you very much. And I appreciate all your help and support and advice.

CHAIRMAN PALESTRO: Thank you.

MEMBER ENNIS: So, it has been great to work with you and get to know you. And particularly I appreciate that from time to time you had an

independent streak. That was refreshing.

Almost every vote here is unanimous. And that could be good, but there could be a need for some fresh new points.

And I appreciate your ability to do that in a collegial kind of way, but still be able to think for yourself, and think outside the box.

CHAIRMAN PALESTRO: Thank you.

MR. EINBERG: Dr. Jadvar?

DR. JADVAR: Chris, I haven't served of course on ACMUI before. This is my first day today. But, I remember maybe a year and a half or two years ago, at an SNMMI meeting I asked, I came to you and talked to you and said, I'm very interested in joining.

And it's wonderful that you remember after all that time, when the time came for this vacancy to be opened up, you actually sent me the email. And I really appreciate your attention.

And I'm very grateful to be here. Thank you.

CHAIRMAN PALESTRO: Thank you.

MEMBER DILSIZIAN: Well Chris, as you know, we met from the scientific sessions at the SNMMI. And I got the pleasure to get to know you here more personally.

And I was blown away with your chairmanship. I mean, you did an admirable job, I have to say. And you kept everything more interesting. You kept us all organized. And your input in many of the topics was fantastic.

And I have the greatest respect.

CHAIRMAN PALESTRO: Thank you. Thank you very much.

MR. EINBERG: Mike?

MEMBER O'HARA: Chris, you've been an inspiration to me. I'm watching you, your leadership style. I think that you have been a leader that anybody in the federal government could learn from.

And I thank you.

CHAIRMAN PALESTRO: Thank you.

MR. EINBERG: So personally, I was here when Dr. Palestro joined the ACMUI. And so, he was sitting in the same seat that Dr. Jadvar is now in.

(Laughter)

MR. EINBERG: So, I've seen him rotate around the table here, to the other end. And the last year and a half he's served as the ACMUI Chair.

And I greatly value his contributions. I've left the group and come back to the current position.

And so, your insight, your leadership to me, is very admirable. And it's greatly appreciated. So, thank you.

CHAIRMAN PALESTRO: Thank you. Thank you very much.

MS. KOCK: And I'll just reiterate what I started to say this morning, which is how much the Commission, and I think Chairman Svinicki's presence here really just sends home the point how much the Commission really values the input of the ACMUI.

But, and I haven't been in this position for long, about six months now. But I've kind of floated in and out of the ACMUI through my career.

And my reflection is that the relationship between the ACMUI and the staff has a healthy tension. But I have to say, coming back to it in these last six months, I felt like the relationship between the committee and the staff is as good as it really has ever been in terms of responsiveness.

I mentioned that this morning. Just there's been a number of quick turnaround things that we've come to you and asked for input on. And you've quickly gotten people together to be respectful and very responsive to us. And we appreciate that.

And while I think that the issues that come

up in medical are always really complex for the -- as we saw this morning, recently I think there's been a number of particularly challenging issues.

And we talked about some of those this morning. That your leadership has just really been critical for us. And I thank you for that.

CHAIRMAN PALESTRO: Thank you very much. Thank you all.

MR. EINBERG: And then Sophie. Don't be shy.

(Laughter)

MS. HOLIDAY: I am not shy. So similar to Mr. Einberg, I think Dr. Palestro, as you started your first term on the ACMUI is when I was first becoming, you know, inducted into my role with ACMUI.

I know as you remember, Ashley was in that role when you first started. And then it, you know, transitioned to me.

And so that means I've seen perhaps four ACMUI Chairmen, since my inception, in the role. Which is now passed onto Kellee Jamerson. And so, similar to when we have management changes here, you see that every chairman has a different style and a different approach.

And what I've been told at the Agency is

that a good manager has that strategic planning. They are always looking at the big picture. They're looking forward.

And I think some of the initiatives that the ACMUI has taken, including and making changes to the bylaws to consider the ACMUI Chairman's role on subcommittees is something that we had not considered in the past. And I think that's something unique that you've brought to the Committee.

And the last thing that I will leave you with is, I'm not sure if you recall, at one point you and I had a meeting. And the message you gave me was, call me on that number that I don't know how you got.

(Laughter)

MS. HOLIDAY: And my response was, I have everyone's number.

(Laughter)

MS. HOLIDAY: Thank you.

MEMBER OUHIB: Dr. Palestro, I think a couple of things that I will always remember is your style of leading admirable. Even though sometimes let's say we have a different idea.

It was very, very appropriate the way, not only the way you presented it, but the way it comes through the whole committee per se. And that, I think,

speaks for itself very, very admirable.

So, I wish you all the best.

CHAIRMAN PALESTRO: Thank you very much. Thank you.

MR. EINBERG: If there are no further comments, we'll turn it back to you Dr. Palestro.

CHAIRMAN PALESTRO: All right. The next item on the agenda, and actually the last item for the open session, is the Xcision GammaPod Licensing Guidance Subcommittee.

Dr. Wolkov, the Subcommittee Chair, will present the report.

MEMBER WOLKOV: Thank you Dr. Palestro. If I can have the next slide?

This is a report on the Xcision GammaPod Licensing Guidance. The subcommittee charge was to review and comment on the draft Xcision GammaPod Licensing Guidance.

The subcommittee members, Zoubir Ouhib, Michael Sheetz, Megan Shober, and NRC Staff Resource, Katie Tapp. Next slide.

We are going to actually spend a little time going through the background since most of us around this table are not familiar with this device.

The GammaPod is a non-invasive

stereotactic radiotherapy system which utilizes Cobalt-60 sources solely for the treatment of breast cancer. There are 25 Cobalt-60 sources in this particular device.

Now the system is very different from the Elekta Gamma Knife stereotactic radiosurgery system. With Gamma Knife we use a head frame for fixation. Or with the icon unit we can use thermal plastics, sort of mold in order to keep the patient rigid during treatment.

Treating breast tissue is obviously a lot different. And what is employed here is a vacuum assisted breast cup immobilization system and stereotactic localization system.

Another difference is the Gamma Knife we're familiar with basically has stationary sources. They will move from place to place, but during the actual treatment, they're static. With the GammaPod, the rotating sources and the collimator carrier is moving during treatment.

Another difference with the Gamma Knife, the table is static at the time of treatment delivery. But with the GammaPod, the table actually moves during treatment. We can have the next slide.

Currently there are two units that are

operational in the United States. One is at the University of Maryland. There it has been in existence the longest.

And more recently, the University of Texas Southwest has started their program. Late next month perhaps, the third program will come onboard, and that's the Alleghany General Hospital program in Pittsburgh.

And within a month or two after that, the University of Ottawa in Canada, will start their program.

The NRC/Agreement States Working Group determined the device should be licensed under 10 CFR 35.1000. Next slide.

Again, for background, it's important to put the duration in perspective. Typically, when treating breast cancer, deliver treatment to the entire breast. And we'll oftentimes treat that low axilla and tangential fields.

And the treatments can vary from what is now one of the more common treatment regimens, which is 42.56 Gy given in 16 fractions, to six and a half weeks of daily treatment, Monday through Friday, five days a week.

An alternative way to treat is with accelerated partial breast irradiation. Which I'll

refer to as APBI in the slides. Next slide, please.

The rationale for accelerated partial breast irradiation is that we may be overtreating a lot of women. Surgical series have demonstrated that it's pretty uncommon to see cancer cells greater than about a centimeter from the tumor bag.

The majority of in breast occurrences occur at the lumpectomy site compared too elsewhere in the breast, despite administration of full breast radiation or omission of whole breast irradiation.

Another reason for popularity for the accelerated partial breast irradiation approach is the convenience of a lot fewer treatments. Then up to six and a half weeks of daily treatment. Next slide.

So current techniques that we're familiar with for APBI. Multiple catheter interstitial brachytherapy, balloon-based brachytherapy like SAVI, interoperative radiation therapy like Introvene, and stereotactic body radiotherapy such as Cyber Knife, or what we'll be discussing for now on, which is the GammaPod. Next, please.

This is what the GammaPod looks like. There is a treatment loader which sits on top of the functional device it contains. It can hold 60 sources. Next slide.

In 2006, the GammaPod was patented by William Regine and Cedric Yu, a physicist at the University of Maryland. In 2007, a 3.5 million dollar NIH grant was given for the development of the GammaPod system.

The first clinical trial was launched at the University of Maryland Medical Center in 2015. And in December 2017, the device was granted FDA clearance. Next, please.

So, let's look a little bit more at the delivery system. The GammaPod unit sits underneath the treatment couch. So, patients are positioned above the sources for treatment delivery.

There are 25 Cobalt-60 sources in the current and probably in future systems. There were 36 sources in the initial system.

The sources continuously rotate during treatment, creating thousands of beam angles and individual beams converge to create an intense focal spot, delivering full dose to the target, while sparing surrounding normal tissue.

There are two collimator sizes, 25 millimeter and 15 millimeters. They dynamically change during treatment.

And we'll contrast this to Gamma Knife or

in the current Icon system, there's a four millimeter collimator, eight millimeter collimator, or excuse me, 14 millimeter collimator and 16 millimeter collimator.

In the only units, a C unit and the B unit, it was a four millimeter, eight millimeter, 14 millimeter, and 18 -- let's see, 14 and 18 millimeter collimator system. So, it's a difference in that as well.

Table motion during treatment enables dynamic dose painting as the target moves across the focal point in three dimensions. Next slide.

At the immobilization system it's very unique. Obviously stereotactic radiotherapy of any type requires a high degree of precise immobilization to ensure accurate dose delivery.

The GammaPod uses a vacuum assisted dual cup system that adheres non-invasively to the breast. The -- a flange that has an adhesive on it that we'll look at in just a bit.

The GammaPod breast cup system provides breast tissue immobilization. And also serves as a stereotactic frame and it enables reproducible set up between imaging and the actual treatment. Next slide.

So how does it work? Patients are custom fit with an appropriately sized inner cup. There are

25 different sizes to the inner cup, five small, ten medium, ten large.

The inner cup is joined by a silicone flange to a rigid outer cup containing an embedded stereotactic fiducial wire. There are three cup sizes for that.

There's adhesive on the flange that helps adhere the device to the patient. And it's attached to a suction pump that will evacuate air from between the two cups to provide stable immobilization. Next slide.

Here are examples of the breast cups. Next slide. And the generated treatment plans are very, very similar in character to what we see with the Gamma Knife. Highly conformal.

If you notice, this patient is in the prone position. So the breast is moved by gravity away from the chest wall. Away from normal tissue such as muscle, rib, heart. Next slide.

The GammaPod employs a patient loader. And actually by having patients in a prone position, it does offer benefit that I alluded to earlier, the breast falls away from the chest wall.

And a -- the GammaPod uses this prone patient loader for both imaging, which is typically done in a different part of the department, on a CT

scan, or from what I just found out yesterday, it can be used with an MRI.

And basically there's a treatment room that the sources are in that GammaPod unit that you saw the picture of. Next slide.

And this is a patient on the loader. And it moves very smoothly to the top of the table. Next slide.

So the patient steps onto the ladder wearing the breast cup. Fits through an aperture in the couch. Securely docked in place.

There's a smooth rotation of the couch from the standing to the prone position. For the image load of the CT scan receives the couch and patient, which is in a position for scanning.

For the treatment loader, the GammaPod receives the couch and patent, which is then positioned for the actual treatment. Next slide.

I'm not going to go through this. But the workflow is somewhat similar to the old Gamma Knife workflow, with obvious exceptions. We tend not to use breast cups for treating brain tumors.

But basically it takes a fair amount of time sometimes to correctly fit the cup. It's critical for immobilization.

CT scanning takes about 20 minutes. Which is probably a little bit longer then the onboard CT scanner that we use with Icon unit.

Treatment planning, about 30 minutes. This is going to be comparable to simple cases for Gamma Knife.

Treatment delivery maybe 30 minutes. Total treatment time could be an hour. Next slide, please.

So how is GammaPod currently used? Well, it can be used in one of two ways. As APBI, five fractions. So some people are looking at maybe giving three fractions delivered every other day.

In discussions with Dr. Nichols at the University of Maryland, I spoke to her, probably now it's been about three weeks ago, there are about 14 patients who have completed treatment with good results.

To be used as a boost technique following the external beam radiation. So you can do it in one fraction as opposed to several daily fractions. That would be regard for boost treatment. Next slide.

This has the opportunity perhaps to replace more invasive types of partial breast irradiation. Dosimetry looks very good.

Logistically it looks like it would be reasonable to do. And there's very good optimization in dose away from critical structures. Next slide.

I'm going to move to the subcommittee recommendations. And in the first section is training and experience.

As I pointed out earlier, the GammaPod is very different then the Elekta Gamma Knife that most of us are familiar with. The subcommittee determined that experience with Elekta Gamma Knife does not assure competence with the GammaPod.

The draft guidance currently does not require attestation for AUs, AMPs, and RSOs who are qualified to use Gamma Knife. The subcommittee recommends attestation for non-board certified AUs, AMPs and RSOs even if they've already are authorized users of other stereotactic radiosurgery units.

The subcommittee recommends the inclusion of a two-year delay for the written attestation requirement for the RSOs to conform with a proposed two year delay for AUs and AMPs currently within the licensing docket. Next slide, please.

The draft guidance currently recommends training on the differences between Gamma Knife and GammaPod for those who are qualified for Gamma Knife.

The subcommittee recommends removing the requirement for Gamma Knife trained individuals, that would be AUs, AMPs, and RSOs to be trained on the differences in the device operation safety procedures, and clinical use of GammaPod compared to Elekta Gamma Knife.

The subcommittee does not feel training on the differences between the Elekta Gamma Knife and the GammaPod provides increased safety with respect to how these devices operate. Next slide.

The draft guidance currently allows residency program directors to provide written attestation similar to 10 CFR 35.600.

The subcommittee recommends removing the ability of a residency program director to provide a written attestation since it's not likely the programs will include GammaPod experience at this time.

And it's unlikely GammaPod will be a standard treatment modality included in most residency programs, certainly in the near term.

The attestation should be restricted to the authorized user for GammaPod. Next slide.

The draft guidance currently allows a physician under the supervision of an authorized user who has been trained in the operation and emergency

response for the unit to be physically present instead of the AU during continuation of patient treatments.

The subcommittee recommends explicit specification of who provides training and operation and emergency response for the physical presence requirement. Next slide.

Associate RSO. The current draft guidance provides guidance for an Associate RSO. The subcommittee recommends not including the ARSO in Part 35.1000 licensing guidance documents, because their roles are outlined in the new part 35 Rule, and addressed in NUREG-1556, Volume 9.

The RSO cannot be replaced by an ARSO. The ARSO involvement confounds the RSO's responsibility. Next slide.

Calibration and spot checks. Currently there is a very, very long description for calibration and spot checks. The subcommittee recommends splitting full calibration and periodic spot checks into two separate sections.

The subcommittee recommends the clear specification of the geometric accuracy and source exposure indicator light spot checks be performed on a daily basis.

The subcommittee recommends deleting the

phrase, in addition too daily QA, from the monthly spot check statement. Next slide.

The draft guidance states the frequency for speed of the table motion and collimator and source rotation and location of the radiation isocenter should be done approximately every six months, while the sealed source and device, SSD registration sheet states that these tests should be performed annually.

The subcommittee recommends resolving the discrepancy between the frequency for speed of the table motion and collimator and source rotation and location of the radiation isocenter. Next slide.

Written directive and source description. The subcommittee recommends adding frequency of fractions to the written directive.

In Section 3.3, the subcommittee recommends replacing the GammaPod Model A in the chemical physical form line with the source models as listed in the SSD registration sheet.

Example, Model INIF-SF-1.0-03-AE for the 25-source configuration. Next slide.

The subcommittee wishes to acknowledge Dr. Elizabeth Nichols, the University of Maryland, and Dr. Stewart Becker, a physicist at the University of Maryland for providing some of the slide presentation

material today, and helping the subcommittee understand this new treatment device that nobody has had experience with on the subcommittee.

At this point I can open this up for questions.

CHAIRMAN PALESTRO: Thank you, Dr. Wolkov for that very comprehensive and thorough presentation. Comments from other members of the subcommittee?

(No response)

CHAIRMAN PALESTRO: Comments or questions from members of the ACMUI? Dr. Ennis?

MEMBER ENNIS: So, you mentioned a discrepancy in a certain QA aspect relating to the table motion and rotation. Which actually sounds to me like potentially one of the most novel and most critical aspects.

Does the committee have a position on what ought in their opinion be to frequency of those checks?

MEMBER WOLKOV: Well, personally, I do. But, I think that question needs to be resolved by the NRC and the OAS Working Group.

Accuracy checks we do on the Gamma Knife daily. It's critical.

MEMBER ENNIS: Um-hum. All right. So I think a year or even six months sounds to me surprisingly

less, not as often as I would have thought something so crucial.

So I was wondering if your subcommittee --

MEMBER WOLKOV: That's correct.

MEMBER ENNIS: Had an opinion on this?

MEMBER WOLKOV: No. We didn't discuss that specifically.

CHAIRMAN PALESTRO: Other questions? Dr. Wolkov, I have a couple of questions for you. In Item Number Three, the subcommittee recommends that the attestation should be restricted to the AU for the GammaPod as opposed to the residency program director.

Can you explain the rationale for that?

MEMBER WOLKOV: Well, there are very, very few programs that offer this currently. And that's one of the challenges that the committee had.

And so by the end of the month there will be two programs operational in the United States. That's the rationale.

MEMBER DILSIZIAN: Let's see if I could follow up on it, I guess. Any new developments will obviously have some time to start.

When we're coming up with rules and regulations, and recommendations here, is it for

present? Or is it for the future?

Because in time, as you know, probably a lot of centers will have this. I just wanted to know if the recommendations are only for the current time?

MEMBER WOLKOV: Well, actually the way I view this, it is for the current time. There is another line elsewhere in the guidance document that talks about the two year delay.

Because it's appreciated that it will take some time to become experienced and for this technology to grow.

CHAIRMAN PALESTRO: I guess when I read this, and I don't want to put words into your mouth or into the mouth of the subcommittee, it almost seems that the program director isn't qualified to provide that written attestation.

And in my mind, --

MEMBER WOLKOV: I can --

CHAIRMAN PALESTRO: Let me rephrase it. I can tell you what I'm really thinking as I read it. It almost sounds as if we don't trust the program director to give written attestation.

And that it should be done by the AU, whereas what I'm thinking is the PD would not give written attestation if it didn't come from the AU.

I don't know if I'm explaining myself properly.

MEMBER WOLKOV: I think you are. And I think the way that I visualize this, and Michael, will you, I believe you had written that comment. But, if you'll allow me to try to explain it the best I can.

At the present time there really is one residency program director who can write a written attestation. There will be more in the future as technology expands and is found more frequently in the departments.

Put it this way, there really is one program director. And at the end of the month maybe there will be two.

So, we're not talking about a lot of programs that have residency directors that can provide a meaningful attestation at this point. But I think that will change over time.

Michael, did you want to comment?

MEMBER SHEETZ: Yes, if I could add to that. In addition to accepting residency program director's attestation on a preset statement is relatively recent with respect to nuclear medicine license programs and radiation oncology programs.

And it facilitates, the residency program

director sees them, the resident in very different modalities, 100, 200, 300, or 400 and 600. Whereas the actual training within the program would be this authorized user for 600, this authorized user for 400.

And so in order to get, you know, the authorized user for 600, initially it's an optimum of 400. So it facilitates one signature for all the modalities within the nuclear medicine or the radiation oncology residency program for that preceptor for that individual.

And so NRC can correct me if I'm wrong, this is sort of a take off of that. This device is so new, there's only two, maybe three or four devices.

It's not going to be integrated any time soon into these residency programs as a new modality. And so we didn't mean to slight or state that a residency program director would not be qualified.

It's just that we did not see an application of the page of it at this point in time. And since this is Part 1000 licensing guidance, at such time that GammaPod becomes a routine modality within radiation oncology residency programs, it could easily be added as a revision to the licensing guidance. It's not rulemaking.

CHAIRMAN PALESTRO: Well, the question --

I'm going to ask Mr. Einberg this question. How easy is it to add something to regulatory guidance?

MR. EINBERG: So, since this is a 35.1000 licensing guidance, we would have to open up the licensing guidance to another revision of that licensing guidance.

But as you probably know, we've done multiple revisions to the Y-90 licensing guidance. And so, it's possible and we can make changes in the future.

And I will turn it over to Dr. Tapp and see if she has anything to state regarding this licensing guidance.

DR. TAPP: Yes. It's not like rulemaking. It does not take years to do. To make a minor change, you can do it relatively quickly.

But relatively quickly is still about six months. That would be probably the fastest we can go through and do a licensing guidance change.

Because we do want to come back to the ACMUI in most cases, unless it's something very minor. We also go to the states and their regions for comment.

So, about a six-month process. But not a whole year.

CHAIRMAN PALESTRO: Thank you.

MEMBER GREEN: Recommendation number one has a built in two-year delay. Can we make that two-year delay in recommendation number three as well?

That will allow more resident programs to get the device. And to bring it into the standard of care.

MEMBER WOLKOV: It certainly would be another way to handle that. Certainly we've looked at the current language within the guidance, licensing guidance.

And the only place where there was mention of the two-year delay was in that earlier number one slide.

VICE CHAIR METTER: This is Darlene Metter. As far as the current standing is that the attestation should be restricted to the AU for the GammaPod, I see in the future perhaps the program directors will be the AUs.

And so, it really should -- I mean, this would then encompass that statement too. So, at this current time I think it, it appears most appropriate.

And in the future, that person will be the program director as more instruments get installed and the experience increases.

So, I think this still is all encompassing.

CHAIRMAN PALESTRO: Okay. Dr. Wolkov, I have another question for you. Under the written directive in source description, the subcommittee recommends adding frequency of fractions to the written directive.

MEMBER WOLKOV: Um-hum.

CHAIRMAN PALESTRO: And my question is, why?

MEMBER WOLKOV: In any written directive you need to have a physician statement as to dose and as to frequency of treatment.

And so that would be standard to a prescription.

CHAIRMAN PALESTRO: Okay. I think that that's one that's understandable. We're not ready to vote on it yet.

But I certainly would recommend that the explanation for that reasoning be added.

MEMBER WOLKOV: Okay.

CHAIRMAN PALESTRO: And again, you know, this is -- and I know you're new to the committee, but this has come up in the past.

As we go back and try to research previous decisions, the rationale for making those decisions and recommendations isn't always clear.

I mean, we've got this very diverse group of individuals on the committee. And while it might be clear to some of us because it's our area of expertise, it may or may not be clear to everyone else.

And in the paragraph below that, in Section 3-3, the subcommittee recommends replacing so forth and so on. Again, my question is, why?

What's the reason for it?

MEMBER WOLKOV: Just so there's no discrepancy in the language.

CHAIRMAN PALESTRO: Okay. I would again, recommend that that be added.

MEMBER WOLKOV: Okay.

CHAIRMAN PALESTRO: And then last, and this may already have been asked and answered. But, if it was, I didn't catch it.

The subcommittee recommends resolving the discrepancy between the frequency for speed of table motion, collimator source rotation and so forth. In one case it's every six months. And in the other case it's annually.

Does the subcommittee recommend which of those two times points?

MEMBER WOLKOV: No. We recommend referral back to the NRC and the OAS.

MEMBER SHOBER: The Working Group.

MEMBER WOLKOV: The Working Group.

CHAIRMAN PALESTRO: Okay.

MEMBER SHOBER: And this is Megan Shober. One of the reasons for that is because none of us have actual, like personal experience with the device.

And I think that one of the people on that Working Group, and you can correct me if I'm wrong, is from Maryland, and knows how these things work?

DR. TAPP: Yes. One of the members of the Working Group is the state regulator from Maryland who did the SS&D. Worked on the SS&D for that device as well as license that device.

So, we'll work with her and determine which -- I know why we recommended it as a Working Group for six months. That's when the manufacturer does the testing.

I'm not sure if the SS&D was just trying to be a little bit less stringent. So, we'll work with her and get that explained too.

CHAIRMAN PALESTRO: Other comments or questions from the ACMUI? Dr. Ennis?

MEMBER ENNIS: Just in terms of the safety issue of the non-AUs stepping away during the treatment. Does the guidance mimic what is currently applied for

Gamma Knife and HTR?

Or does it differ from this?

MEMBER WOLKOV: Well, it's very similar. But, it does not -- the guidance, the licensing guidance statement does not really discuss who is responsible for, if you will, teaching emergency procedures.

In our center we have a physicist who will do that. That's -- the language is missing from this document. So we wanted to have it specified.

MEMBER ENNIS: And is there anything in the guidance about if treatment is interrupted that the authorized user has to return?

If it's being restarted, the authorized -- does the guidance talk about that language in there?

MEMBER WOLKOV: I'm not familiar with it. I don't recall. I don't think it does.

DR. TAPP: It's physical presence currently in draft mimics the Gamma Knife's, the current Gamma Knife's that was recently revised.

MEMBER ENNIS: Okay.

CHAIRMAN PALESTRO: Mr. Ouhib?

MEMBER OUHIB: Yes. Two comments. You know, I'd like to go back to item number three. Would potentially having the ability of a residency program

director and the authorized user to provide a written attestation.

By simply making, adding the authorized user in there to make sure that we're not having any second thought about the program director, per se. Would that be satisfactory?

MEMBER ENNIS: So would it be or, or and?

MEMBER OUHIB: And.

MEMBER ENNIS: So you want both to have to attest?

MEMBER OUHIB: The authorized users will probably, I mean, is aware of whether that individual has really met the requirement. The program director is sort of like in charge of the program itself.

So there is like a communication between the administrative portion and the technical portion.

MEMBER WOLKOV: Katie, do you want to address that?

DR. TAPP: Sure. If I may, first that would go above and beyond what's currently in Part 35. Part 35 allows a residency director to attest, it committed to that part earlier for other reasons.

I think one of the things that the Working Group talked about with the residency director, is as it's not applicable now, they recommended removing it

because if you look at the guidance, it's about two pages that kind of spell out all the different options for training and experience, just like all modalities.

So it was very complicated. So, I think part of it was just to try to simplify it and make it a little bit cleaner.

Right now since that is not an option that we'd likely use for the foreseeable future. Since there's only one institution, the residency program. I'm not sure if Texas has a residency program.

This is not wide spread enough yet where that option is going to be used.

CHAIRMAN PALESTRO: I'm sorry, Dr. Tapp, could you repeat that. I didn't quite follow what the Working Group said it is.

DR. TAPP: Well, the Working Group has not analyzed the ACMUI's recommendations yet, because they're not final.

But I believe when I saw the recommendation, I understood that currently that would be a use to have. And since the training and experience is very complex, it would be fine to take it out to try to simplify it in the 35.1000 licensing guidance.

As right now we wouldn't expect residency directors to be providing the attestation.

CHAIRMAN PALESTRO: Okay. Is there a question about that? Dr. Howe?

DR. HOWE: Yes. The current Part 35 requirements that a residency program sign attestation. But that the real authorized user, who is qualified to use the device, has to agree to the attestation.

So you would have the authorized user agreeing to the attestation and you would have the program directors providing the attestation.

And I guess my question was, you've indicated that there is one residency program now that would have the device.

Would you be comfortable with that program director with the authorized user also agreeing to the attestation to submitting the attestation?

Because that's what our current regulations are. And one reason we went to the residency director is we found that some authorized users were not that comfortable signing the attestation.

Because they feel it's their responsibility with that if the new individual doesn't perform well in the future. So they would rather have that responsibility put on the residency program.

But essentially if you have one residency

program now, the decision is, would you be comfortable with that one residency program director with the requirements that we currently have in 690 for residency program director to sign?

I don't think you need two, or three, four, five, ten. Would you be comfortable with that one?

And I think that should be the consideration.

CHAIRMAN PALESTRO: Okay. Other comments or questions? Comments or questions from any of the attendees in the room?

(No response)

CHAIRMAN PALESTRO: Comments or -- oh, I'm sorry. Dr. Ennis?

MEMBER ENNIS: So I just want to understand this. Again, on this issue with the program.

So right now University of Maryland residents coming out of training in two years or Southwestern in three or four years, they would have an overall attestation of all their uses through their program director.

But would have to have a separate attestation from the AU who trained them in GammaPod? Is that what we're saying?

MEMBER WOLKOV: I think the answer to that

is yes.

MEMBER ENNIS: Just my personal opinion, it feels unwieldy and in a relatively short period of time is going to need to be modified.

I'm not sure the gain of the fact that there aren't programs now is worth it.

MEMBER WOLKOV: Um-hum.

MEMBER ENNIS: You know, not strongly, but just my personal.

CHAIRMAN PALESTRO: Mr. Sheetz?

MEMBER SHEETZ: I guess the concern is GammaPod is so new that the residency program director may not be an authorized user, or may not even be knowledgeable in GammaPod.

So how can we have that person sign off on an attestation?

MEMBER ENNIS: So, I mean, right now I would say -- I mean, if the residency program director might not be able to do this at all, or the GammaPod at all.

But he or she is overall an AU to describe the training. And then okay, I'll sign off on it.

MEMBER SHEETZ: But that doesn't -- let's say the program director did have brachytherapy training as part of their training at some point in

their career.

MEMBER ENNIS: But they don't have the Gamma Knife experience, and they're still signing off on Gamma Knife all the time.

And I don't personally have a problem, see a problem with that kind of system.

MEMBER SHEETZ: No. The program of Gamma Knife does not allow for these program directors to sign off. It must be an AU.

MEMBER ENNIS: I see. Okay. Oh, really?

MEMBER SHEETZ: Yes. So we're talking about 400 and 600 for radiation oncology.

MEMBER ENNIS: Uh-huh. And this is --

MEMBER SHEETZ: And for 100, 200, 300 for nuclear medicine residence programs for radiology residents.

MEMBER ENNIS: So this is more than what we require for Gamma Knife then?

MEMBER SHEETZ: Well, I'm not sure what --

DR. TAPP: Perfexion Icon.

MEMBER ENNIS: Right.

DR. TAPP: That's at 35.1000. For their traditional Gamma Knife, that would allow the program director.

MEMBER ENNIS: So but for 1000 Gamma Knife it's not a program director it's AU?

DR. TAPP: At this time. The new Part 35 had not been added to the new for Perfexion Icon 35.1000 document for the program director.

That may have been just because of timing of when that rolled out in the tool.

MEMBER ENNIS: Okay.

CHAIRMAN PALESTRO: Any other comments or questions? So Dr. Tapp, just again for clarification.

So there is president for -- precedent, excuse me, for Dr. Wolkov's recommendation, or the subcommittee's recommendation?

DR. TAPP: It would mimic the current Icon perfexion guidance.

CHAIRMAN PALESTRO: Okay. Again, any questions or comments from attendees here in the room?

(No response)

CHAIRMAN PALESTRO: Questions or comments from anyone on the bridge line?

(No response)

CHAIRMAN PALESTRO: All right. Hearing none, it is time for a motion regarding the subcommittee's report.

MEMBER ENNIS: Motion to approve.

CHAIRMAN PALESTRO: I had asked, or we had discussed, and is that a motion to approve with the amended report?

MEMBER ENNIS: Yes.

CHAIRMAN PALESTRO: Okay. Mr. Sheetz?

MEMBER SHEETZ: Second.

CHAIRMAN PALESTRO: All right. Any further discussion? Dr. Metter?

VICE CHAIR METTER: Can we sort of get a summary of amendments? Could we see what the final amendments are before we approve the report?

CHAIRMAN PALESTRO: Could you read the recommendations if you would?

VICE CHAIR METTER: But there were also amendments.

CHAIRMAN PALESTRO: Well, the amended recommendation.

VICE CHAIR METTER: Okay.

MEMBER WOLKOV: The amended recommendations for the written directive and source description, well, I do not have the language. I did not write down any language.

(Off mic comments)

MEMBER WOLKOV: But, the intent is that the subcommittee recommends adding frequency of

fractions to the written directive and then put in a comment as to the rationale for that. Which is going to be that script should include dose and frequency of treatment.

VICE CHAIR METTER: Okay. That's fine.

MEMBER WOLKOV: Okay. And I couldn't tell if there was an amendment that was requested for the Section 3.3. The question was asked about why substitute the model name for the GammaPod Model A.

And that was to take care of any discrepancy in the current language. So, there's -- that was when it's a chemical and physical form line. And the other is an SST registration sheet.

So basically it was to have more consistent language.

MEMBER SHOBER: This is Megan Shober. With that specific recommendation, the GammaPod Model A is act -- is the device name. And then the INIF, that number, that's the source model.

And so when you're putting it on the license, you actually want to describe the characteristics of the source in that chemical form section.

So we just want it to reference the actual sealed source and not the device name. Does that make

sense?

VICE CHAIR METTER: Okay. That helps.

CHAIRMAN PALESTRO: Then the rationale, is it in order to maintain consistency in language? Is that correct?

MEMBER SHOBER: It's to describe the sealed source and not the device. The device gets described in the authorizing section of the license.

But the chemical physical form should be describing the sealed source.

VICE CHAIR METTER: Thank you for explaining. That makes sense.

CHAIRMAN PALESTRO: All right. Dr. Wolkov, if you will allow me. For the first one, the subcommittee recommends adding frequency of fractions to the written directive because the written directive should include dose and frequency.

Is that acceptable?

MEMBER WOLKOV: Yes. Um-hum.

CHAIRMAN PALESTRO: Okay. And the second part, Section 3-3, so forth and so on, in order to describe the sealed source rather than the device. I added that at the end.

Is that correctly stated? Ms. Shober?

MEMBER SHOBER: Yes.

CHAIRMAN PALESTRO: Okay. Any further discussion or comments? Dr. Metter?

VICE CHAIR METTER: No comment.

CHAIRMAN PALESTRO: That answers your questions?

VICE CHAIR METTER: Yes. It does.

CHAIRMAN PALESTRO: Okay.

VICE CHAIR METTER: I just wanted a clarification of what we're voting on.

CHAIRMAN PALESTRO: Okay. That's fine. That's good. All right. So we have a motion that was seconded.

Okay. And Dr. Ennis moved, seconded by Mr. Sheetz. Any further discussion?

(No response)

CHAIRMAN PALESTRO: All in favor?

(Silent voting)

CHAIRMAN PALESTRO: Any opposed?

(Silent voting)

CHAIRMAN PALESTRO: Passed unanimously. All right then, double check. That concludes today's open session.

Closed session will begin at 3:00 p.m. Thank you all.

(Whereupon, the above-entitled matter went

off the record at 2:34 p.m.)

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April 29, 2019

Christopher J. Palestro, M.D.
Chair, ACMUI
U.S. Nuclear Regulatory Commission

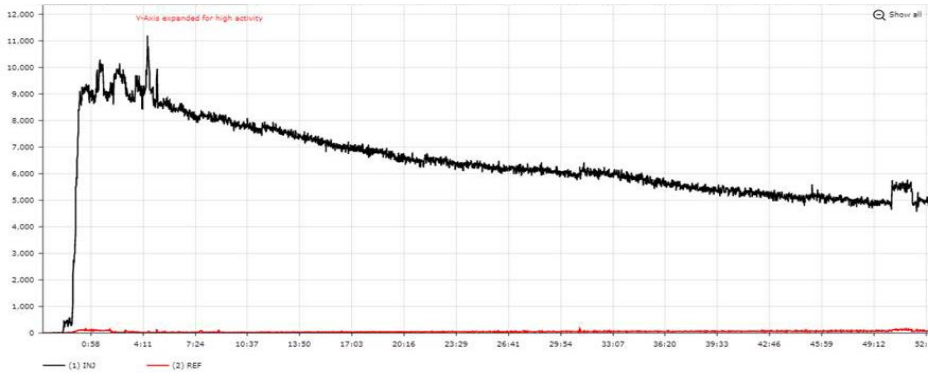
Re: Example Infiltrated PET/CT Case

Dear Dr. Palestro,

Earlier this month, I presented to the NRC and the ACMUI on the topic of infiltrations. I showed that infiltrations occur during nuclear medicine injections at a rate higher than during injections in similar processes, such as chemotherapy intravenous injections. I showed that infiltrations negatively affect the quality and quantification of nuclear medicine diagnostic studies and exposed patients to unintended radiation exposure. I also showed that when centers monitored their injections and used quality improvement processes, they could dramatically improve their infiltration rates. At the conclusion of my presentation, you created a Subcommittee to review the 1980 NRC policy that exempted infiltrations from being reported as medical events, because they were thought to be nearly impossible to avoid during nuclear medicine intravenous injections.

Recently, we became aware of a PET/CT study and repeat study that involves an infiltration. We are publicly sharing this information with the ACMUI to reinforce the negative effects an infiltration can have on a patient.

During the week of April 22, Lucerno's Lara® System alerted one of our customers to the fact that a patient had what appeared to be a significant amount of excess radiotracer near the injection site (see time-activity curve below).



The technologists, aware of this information **before** they put the patient on the PET table, included the forearm injection site in the PET image field of view.

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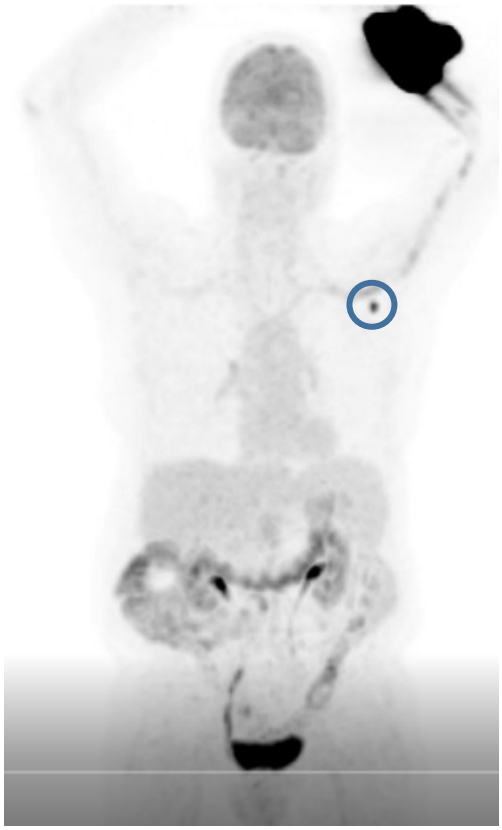
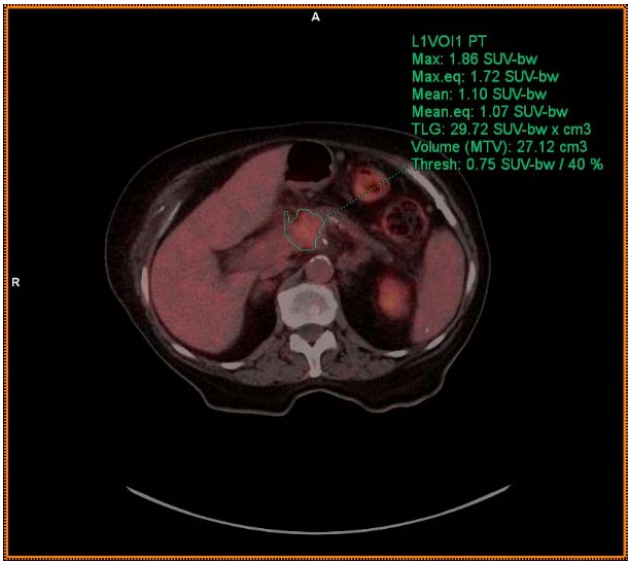
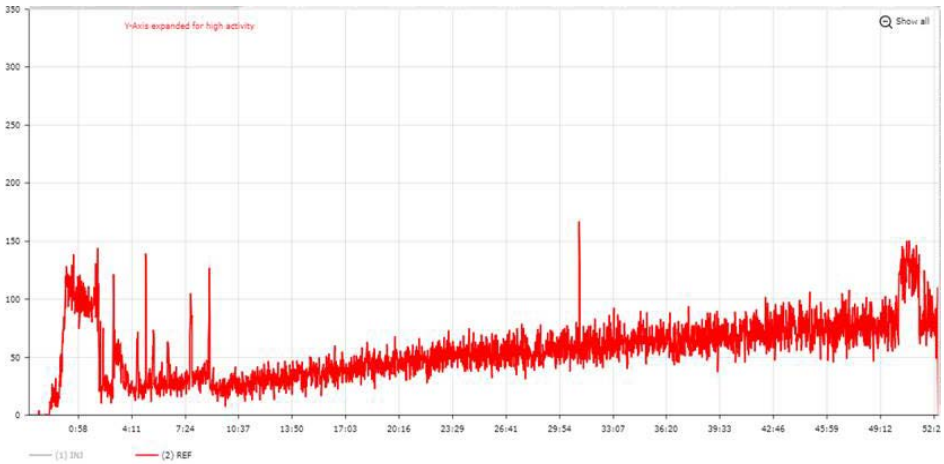


In a screen shot taken from a maximum intensity projection video (left image), the patient's left forearm appears to have been severely infiltrated. A lymph node under the injection arm (in blue circle) shows activity - likely as a result of the infiltration. The patient's pancreatic tumor had an SUV of 1.86, as you can see in the axial image (below).



The time-activity curve below shows a "zoomed-in" view of the reference arm sensor results from the excess radiotracer time-activity curve above. As you can see, the reference arm sensor reveals an increasing count activity throughout the uptake period. This indicates that the radiotracer is being infused over the entire uptake period rather than its intended injection as a bolus. This lack of clearance in the circulatory system reduces the PET image sensitivity. Also note that the reference arm counts are approaching 100 by the time the uptake period ended.



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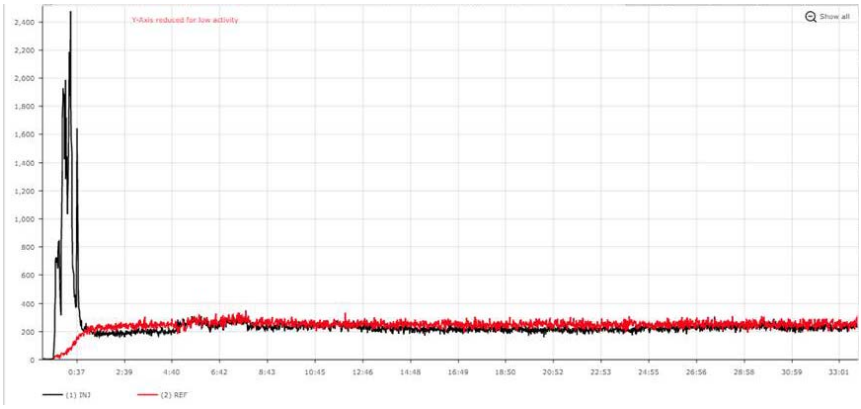
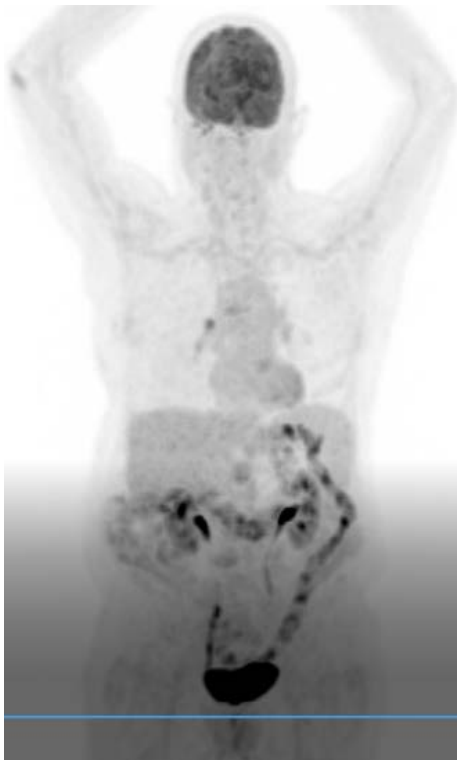
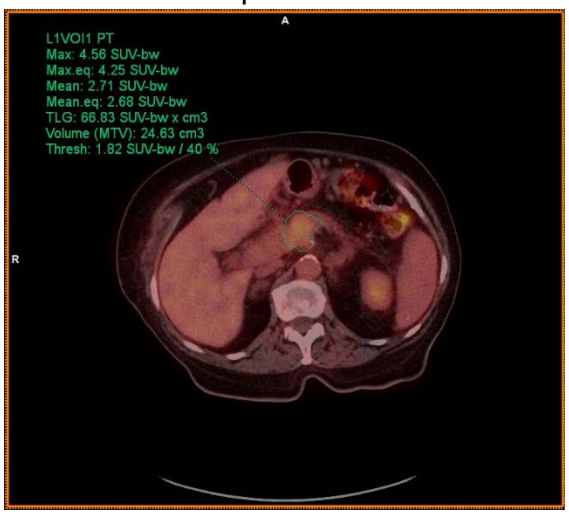
The following day, the patient came back to repeat the PET/CT study. Imaging parameters were held as constant as possible to assess the role that the infiltration played in the quality and quantification of the image. As you can see from the time-activity curve below, the repeat injection appears to be ideal.



The bolus injection is delivered within the first 40 seconds and the counts in the injection arm match the counts in the reference arm for the remaining uptake period. Note that the reference arm counts reach over **200** counts almost immediately. The dose in both injections was slightly over 10 mCi and the reference arms should show the same amount of counts in both studies if both injections were done ideally.



For the repeated PET/CT study, the patient was injected in the left antecubital fossa (inside of the elbow). In the image to the left, note that there is no uptake in the injection arm lymph node. This confirms that the activity in the node from the previous day was likely the result of the infiltration being cleared by the lymphatic system. The axial image below shows the pancreatic tumor SUV of 4.56, indicating that the infiltration resulted in a nearly 60% understatement of the pancreatic tumor SUV.



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This case came from a center that has successfully focused on reducing their infiltration rate (from 13.6% to 2.5%). In centers that are not monitoring injection quality and are using a routine (base of skull to mid-thigh) imaging field of view, interpreting physicians would have known they had a poor-quality image and may have suspected an infiltration, but would not have known the cause of the quality issue. For an infiltrated patient in a center that is not monitoring the injection quality, they may have had an additional procedure to investigate their lymph node activity. It is also unlikely that the patient would have had their PET/CT study repeated; in many centers today, even when infiltrations are seen on the image, the study is not repeated. Based on estimated infiltration rates, it is likely that over one hundred of these cases occur every day in the US and no one knows they are happening.

In addition to the negative effect that this infiltration had on the patient's diagnostic study, the patient also received unintended exposure to their forearm tissue. Based on the quantitative effects, it is likely that more than 8 mCi were injected into the forearm tissue. Once we gather additional information from the center, we can estimate the effective dose equivalent to the tissue.

By eliminating the 1980 policy that exempted infiltration reporting and therefore ensuring that centers report infiltrations that exceed Subpart M limits, the NRC will be encouraging providers to monitor injection quality. Monitoring and required reporting will lead to increased attention on this critically important process and to improved results through quality improvement processes. These efforts will result in fewer overall infiltrations and fewer infiltrations that exceed Subpart M reporting limits. Reducing infiltrations will improve patient safety and the accuracy of nuclear medicine diagnostic studies.

Sincerely,

Ron Lattanze
CEO

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July 8, 2019

Maryann Ayoade
Health Physicist, Office of Nuclear Material Safety and Safeguards

Re: Estimated Equivalent Dose to Tissue from Radiotracer Infiltration

Dear Maryann,

As promised in our letter to Dr. Palestro dated 4/29/2019, we have estimated the equivalent dose resulting from the previously reported radiotracer infiltration. We ask that you share this new information with Dr. Palestro and the subcommittee investigating the 1980 policy that exempts infiltrations from being reported to the NRC.

The hospital's nuclear medicine trained radiologist analyzed the PET image data and found that when using a threshold of 10% of SUV_{max}, the infiltrated activity was 3.51 mCi within 86 cm^3 in the left forearm. The radiotracer injection consisted of 10.22 mCi in 1.5 mL. Through analysis of dynamic activity measurements recorded near the injection site throughout the uptake time, as well as the static measurements from PET data, we estimate that initially the entire injection was paravenous. We estimate that the equivalent dose to the arm tissue for this patient was 4.9 Sv.

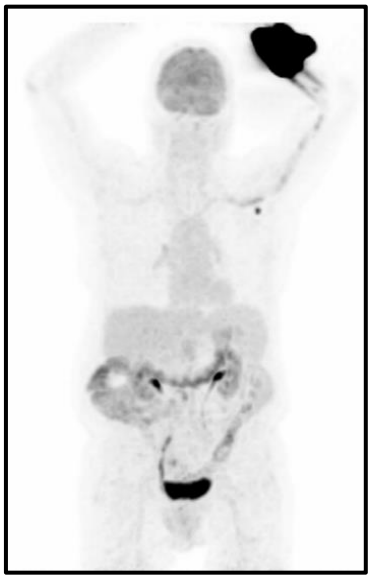

Figure 1. Maximum intensity projection view from PET images.

Our estimation considered the ways in which the infiltrated activity would change throughout the 62-minute uptake time. Initially, the infiltration would comprise a relatively small volume of concentrated radiotracer. Over time, this volume would expand through the interstitial space, undergoing changes in both overall volume as well as heterogeneity of activity concentration within that volume. This process of expansion is complex and dependent on both the patient as well as the location and nature of the infiltration. We modeled the expansion process for this infiltration in order to estimate the dose.

Our model used an exponential function to represent the way in which radiotracer diffused within the interstitial fluid. Additionally, we modeled concentration within the infiltrated volume as an exponential with maximal concentration located at the SUV_{max} voxel at imaging time. We assumed an initial infiltrated volume of 3 cm^3, expanding to 86 cm^3 as measured at imaging time.

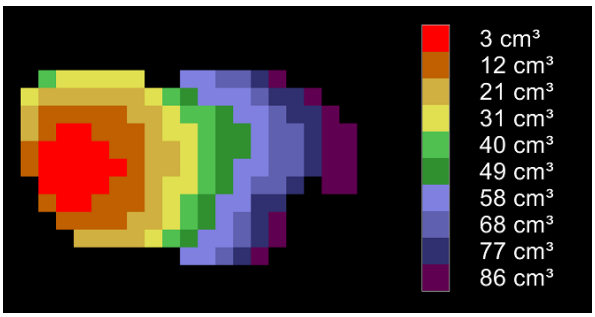

Figure 2. An X-Y view of the infiltrated tissue segmented by volume.

Since the tissue nearest to the initial infiltration site would be exposed to the highest concentrations of radiotracer over time, we chose to focus our analysis on this area.

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Based on the dynamic activity measurements taken throughout the uptake time, we estimated the entire activity (10.22 mCi) was initially infiltrated within the 3 cm^3 volume. From PET data, we know the activity present within the same volume at imaging time (0.35 mCi). Using our radiotracer diffusion model, we calculated activity over time within the 3 cm^3 volume. We used Monte Carlo simulation to estimate the equivalent dose from 1 mCi of ^{18}F to the 3 cm^3 volume (Fig. 3) for 1 minute (32.7 mSv/min/mCi). By applying this dose rate to the activity over time, we calculated equivalent dose over time, which was then integrated to find total equivalent dose (4.9 Sv) (Fig. 4)

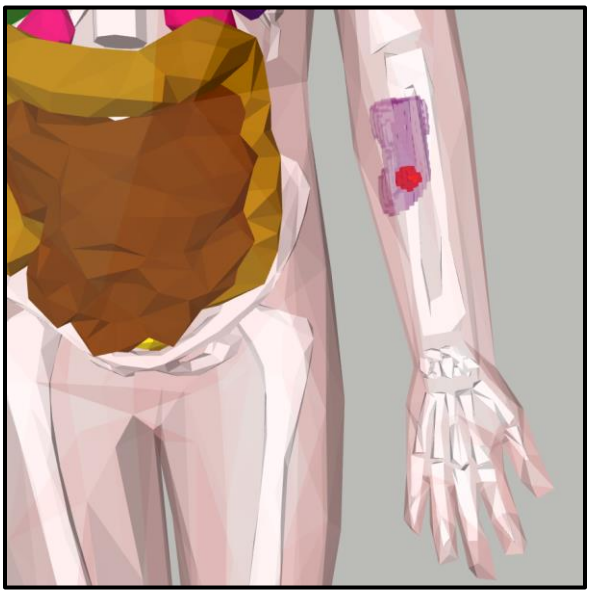

Figure 3. 3D model showing the total infiltrated volume geometry (86 cm^3, purple) and the 3 cm^3 volume used for analysis (red).

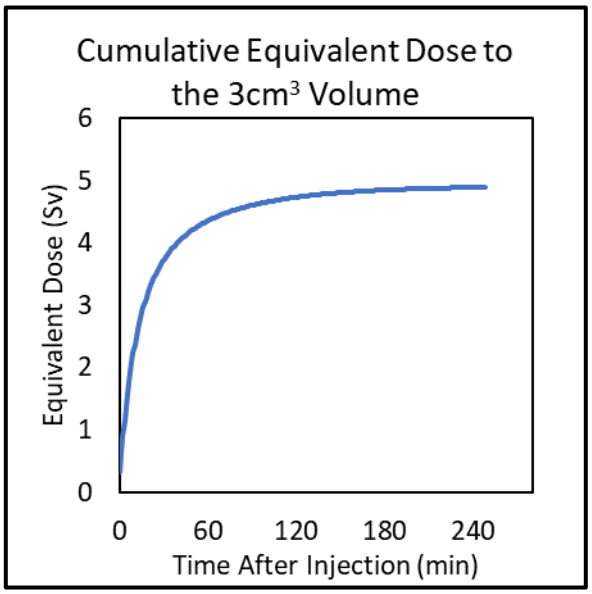

Figure 4. Cumulative equivalent dose to the 3 cm^3 volume over time.

This analysis demonstrates that a diagnostic radiotracer infiltration can result in high equivalent dose to the patient's tissue—exceeding the Subpart M reporting limits in this example by nearly 10 times. This result is conservative because it does not consider the effects of the infiltrated activity outside of the 3 cm^3.

Based on our experience in monitoring diagnostic nuclear medicine injections, we believe that patients are frequently experiencing infiltrations that exceed the reporting limit.

Josh Knowland
VP, Product Development
Lucerno Dynamics, LLC

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July 10, 2019

Christopher J. Palestro, M.D.
Chair, ACMUI
U.S. Nuclear Regulatory Commission

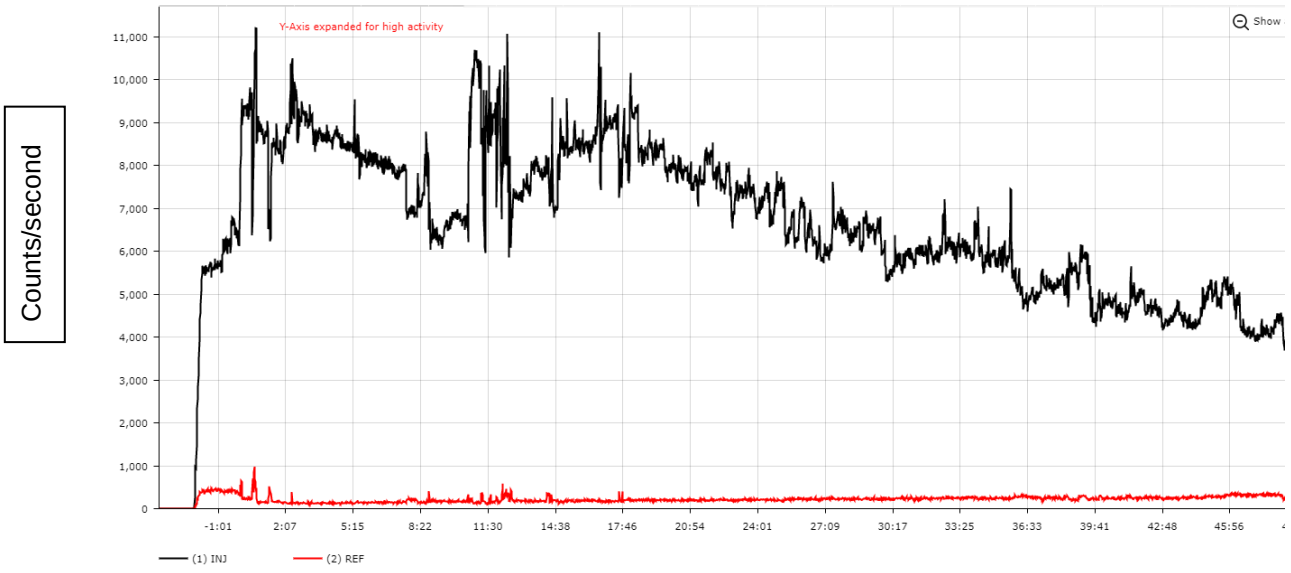
Re: Another Example of an Infiltrated PET/CT Case

Dear Dr. Palestro,

It was a pleasure seeing you at SNMMI last month. Again, thank you, Dr. Metter and Ms. Martin for providing an update to the SNMMI members during the meeting.

I am writing to you today to share yet another example of a significant infiltration. Please share this information to the subcommittee reviewing the 1980 policy that exempted infiltrations from being reported. It is understood that this information would be available to the public for review.

At the end of June, the Lucerno Lara® System alerted one of our customers to the fact that a patient had what appeared to be a significant amount of excess radiotracer near the left antecubital fossa injection site. (See time-activity curve below.)



Uptake time in minutes from injection through removal of the Lara® System

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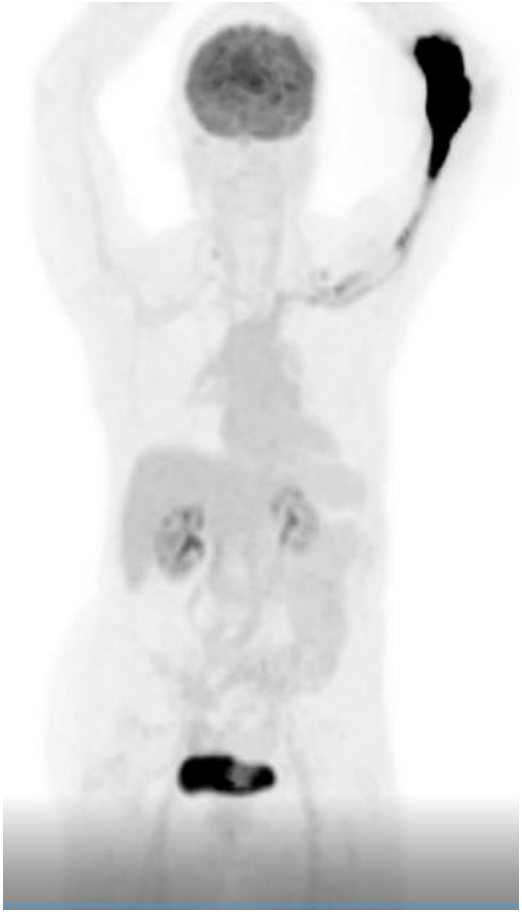
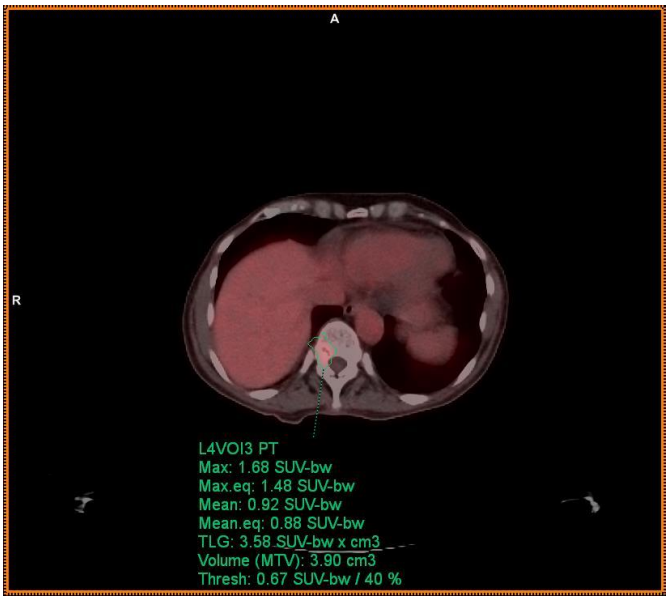
In the time-activity curve above, the black injection sensor curve indicates the possibility of significant radiotracer presence near the injection site. The red sensor curve indicates radiotracer in the reference arm. The technologists, aware of this information **before** they put the patient on the PET table, made sure to include the injection site in the PET image field of view.

In a screen shot taken from a maximum intensity projection (MIP) video as seen in the image to left, the patient's left arm appears to have been severely infiltrated. One of the patient's metastatic lesions had an SUV_{max} of 1.68 and an SUV_{mean} of 0.92. It is barely visible within the region of interest shown in the axial image (below).





The time-activity curve below shows a "zoomed-in" view of the reference arm sensor results from the excess radiotracer time-activity curve above. As you can see, the reference arm sensor reveals an increasing count activity throughout the uptake period. This indicates that the radiotracer is being infused over the entire uptake period rather than its intended injection as a bolus. This lack of clearance in the circulatory system reduces the PET image sensitivity. Also note that the reference arm counts have reached ~ 310 counts per second by the time the sensors were removed.

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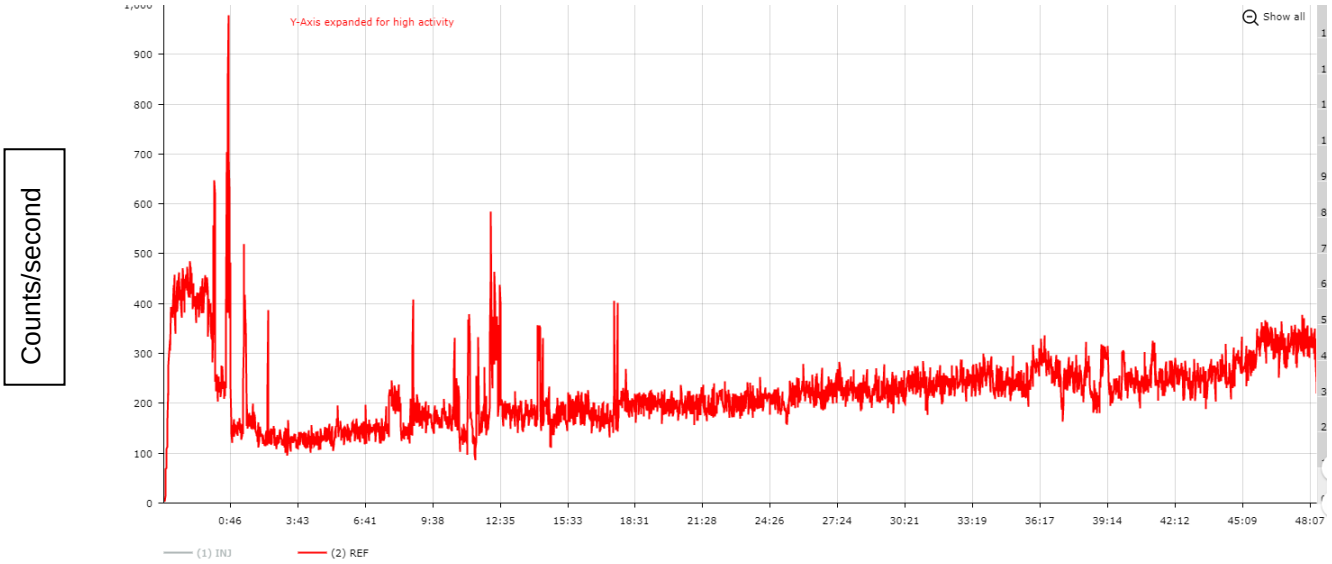
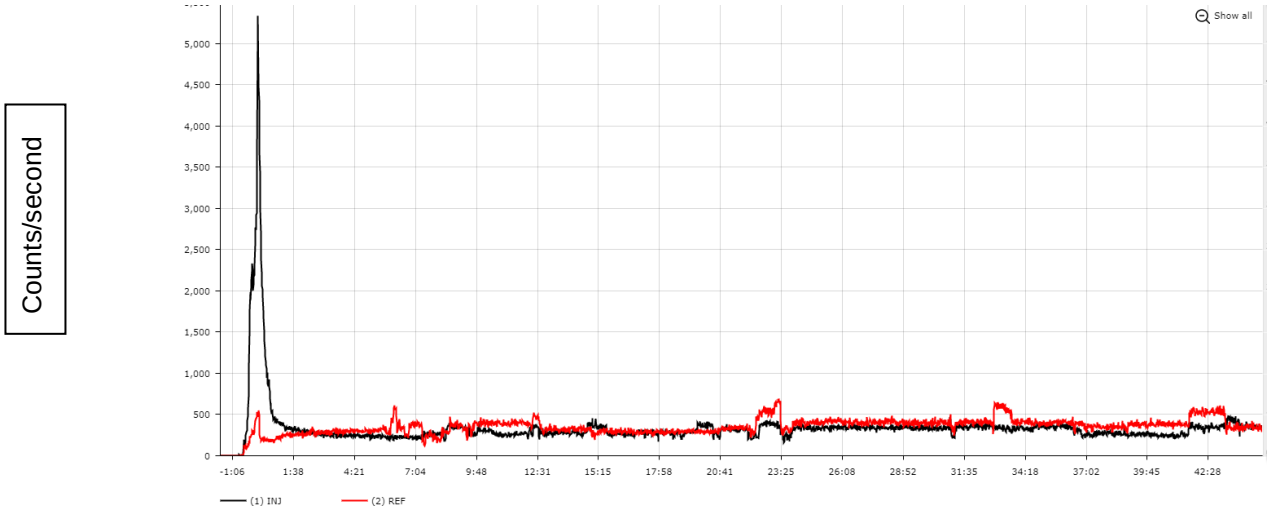


Uptake time in minutes from injection through removal of the Lara® System

Three days later, the patient came back to repeat the PET/CT study. Imaging parameters were held as constant as possible to assess any adverse effects the infiltration caused in the quality and quantification of the image. As you can see from the time-activity curve below, the repeat injection appears to be nearly ideal.



Uptake time in minutes from injection through removal of the Lara® System

The bolus injection is delivered within the first 60 seconds and the counts in the injection arm match the counts in the reference arm for the remaining uptake period. Note that the reference arm counts reach approximately 350 counts per second almost immediately,

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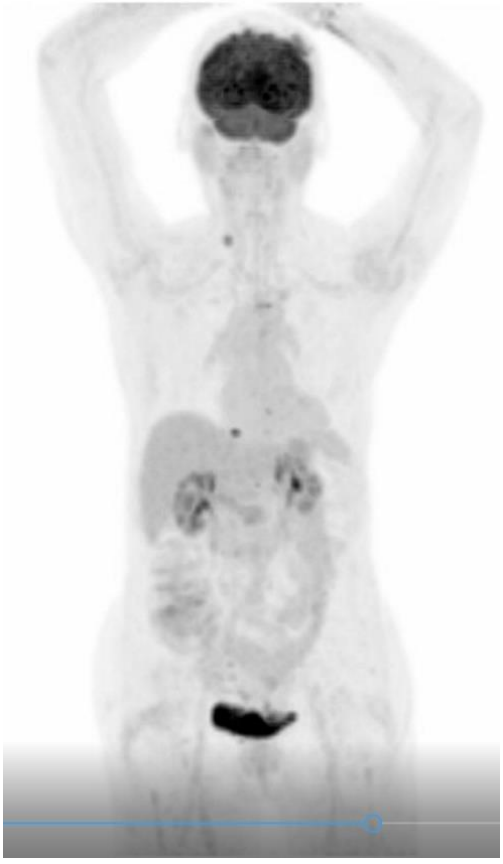
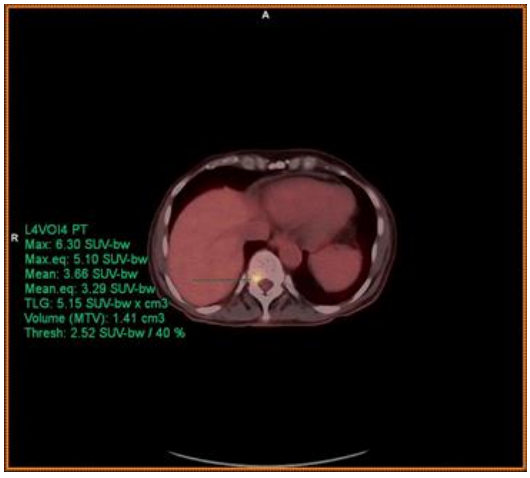
despite the fact that the injected dose was ~7% less than the dose injected during the infiltrated case.



For the repeated PET/CT study, the patient was injected in the left hand. Note the visibility of the metastatic lesions in the MIP image to the left, as compared to the previously shown infiltrated MIP image. The axial image below shows the same previously imaged metastatic lesion this time with an SUV_{max} of 6.30 and an SUV_{mean} of 3.66, indicating that the infiltration resulted in a nearly 73% understatement of the lesion SUVmax.



The center has confirmed that this patient has metastatic breast cancer. The FDG PET/CT study was performed to assess her response to treatment. An assessment based on the infiltrated scan would have erroneously concluded that the disease was responding favorably to the current treatment regimen. A revised assessment based on a high-quality study showed the disease was recalcitrant.

This case is yet another example of how infiltrated diagnostic radiopharmaceuticals can adversely affect both the quality and the quantification of a nuclear medicine study. My team is now waiting for the center to provide information to help us estimate the effective dose equivalent to the arm tissue caused by this unintended exposure of radiation. As with the previous infiltration I forwarded to the NRC and you in April, once we estimate the radiation exposure, we will share this information with you. Based on some preliminary estimates, I suspect this infiltration will also have exceeded the NRC reporting limits. This patient and the previous April patient have provided patient consent to their Nuclear Medicine Physicians to publish their cases and share their images.

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Thank you for your continued interest in this topic. It is my intent to continue to share these cases and additional supporting evidence with the NRC, you, and your subcommittee. I am providing this information to reinforce that patients are being severely infiltrated at a high frequency every day in the United States. Additionally, I believe that you and your subcommittee have the ability to improve the infiltration issue by requiring infiltrations that exceed the reporting limits to be reported to the NRC. Once providers are required to report infiltrations that exceed the 0.5 Sv limit, they will begin monitoring their injections. Monitoring will lead to process improvement and a reduction in the injection issues that compromise patient safety and the accuracy of nuclear medicine diagnostic studies used to help guide care.

Sincerely,

Ron Lattanze
Chief Executive Officer

		April Case	June Case
Patient Weight	kg	72.58	52.16
Injection Method		Manual	Auto Injector
Injected Activity	mCi	10.22	9.99
Injected Radiotracer Volume	mL	1.50	4.00
Injected Flush Volume	mL	30.00	41.00
Imaging Time	min	62.00	62.00
Estimated Total Infiltration Activity @ Imaging Time	mCi	3.51	1.10
Estimated Total Infiltration Volume @ Imaging Time	cm3	85.76	42.47
TAC Based Reabsorption Rate (half-life)	min	55.9	27.6
Estimated Initial Infiltration Activity	mCi	10.22	7.69
Estimated Initial Infiltration Activity	%	100%	77%
Average Impact to SUV	%	-62%	-63%
Estimated Worst Case Volume	cm3	3.00	6.16
Estimated Worst Case Initial Activity	mCi	10.22	7.69
Estimated Worst Case Imaging Time Activity	mCi	0.46	0.51
Worst Case Dose Rate	mSv/mCi/min	26.3	14.1
Estimated Best Case Volume	cm3	31.50	42.75
Estimated Best Case Initial Activity	mCi	10.22	7.69
Estimated Best Case Imaging Time Activity	mCi	2.09	1.13
Best Case Dose Rate	mSv/mCi/min	3.44	2.64
Estimated Worst Case Total Equiv. Dose	Sv	4.92	2.23
Estimated Best Case Total Equiv. Dose	Sv	1.39	0.67

Jackson W. Kiser, MD
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July 3, 2019

Dr. Palestro
Chairman of the Advisory Committee on the Medical
Use of Isotopes
Nuclear Regulatory Commission

Dear Dr. Palestro:

Good day. I am the Medical Director of molecular imaging at the Carilion Clinic in Roanoke, VA. I am aware the ACMUI and the NRC are re-evaluating policy language put forth in 1980 regarding exempting providers from reporting requirements in the event of radioisotope extravasation/infiltration. As you recall, that policy was based on an opinion that these events "happen frequently and are virtually impossible to avoid". I am in agreement that this stance should be reconsidered.

For the past several years, our practice has been using a device that allows us to monitor our injections during PET-CT procedures when administering the intravenous isotope. The device consists of a PET detector crystal that is placed in proximity to the injection site and monitors the delivery of the isotope in real time and can alert the radiologist as to the possible occurrence of an infiltration. For all the years I have been in practice, when I found a patient to have a significant infiltration, I would have the patient return on another day for a repeat scan. Prior to using this new device, I had to rely on visual evaluation of this by placing the injection site, whenever possible, in the imaging field of view. Now with this device, we scan patients with the injection site out of the field of view.

This device has also been instrumental in one of our QA/QC projects where we monitored our technologists for infiltrations over a period of time and found a rate of infiltration of about 13%. When we did an analysis, with statistical review of the data, we had the technologists revise their injection and IV placement techniques. These changes were driven by infiltration associative factors identified by these data. With these modifications, the technologists were able to get their infiltration rate down to about 2%. At the current time,

our infiltration rates are less than 2% and we continue to monitor our technologists going forward.

It has been my stance in practice that when in a test-retest environment, it is critical that all the input parameters for a given test be reproduced at the time of retest to mirror those at the time of the initial test. One of these parameters is knowledge that the radioisotope is delivered systemically. When there is a large infiltration, this can impact the accuracy of the SUV measurement. We have had several cases that exemplify this. Just in the past week, we had a patient returning for follow-up for metastatic cancer. We had a severe infiltration which required that the patient return for repeat scan. The SUVs that were measured on the infiltrated scan suggested a partial response to therapy but the repeated scan without infiltration indicated stable and possibly progressive disease.

I hope that you and the review committee will consider revising the current position on infiltrations. If large infiltrations that exceed NRC reporting limits are required to be reported then providers will begin monitoring their injection quality and implement QA/QC projects like we did to improve our process. This will result in improved imaging, better patient care, less waste, and will also improve patient safety.

Respectfully submitted,

Jackson W. Kiser, MD

CARILION CLINIC

Eddie George

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Dr. Christopher Palestro
Chairman of the Advisory Committee
Medical Use of Isotopes

July 19, 2019

Dear Dr. Palestro,

I want to share with you my experience and thoughts following the diagnosis and treatment for Stage 4 Lymphoma. I am not in the medical field and quite frankly, had basically no experience with cancer or cancer treatment in my 56 years. However, I have gained considerable knowledge and experience in this area over the past twelve months.

On the afternoon of July 17, 2018, I had a PET scan at Wake Forest Baptist in Winston Salem, NC. During the twenty-minute ride home from the scan, I got a call from Dr Vaidya, my oncologist, advising me that I would begin chemo at Baptist the following morning. Based on the scan, my cancer was so extensive (from my neck to my left thigh) and aggressive that treatment must be immediate. Also, the scan found a crack in my lower back (hip) believed to be a result of the cancer and it caused great concern. I checked into Baptist at 7:45am the following day and life was changed.

I was infused with chemo drugs (R-EPOCH) for five straight days (in the hospital) and then allowed to "recover" the next sixteen days. This twenty-one-day cycle would repeat six times over the next five months. On August 23rd (after round two), I had a second PET scan at Baptist to verify my progress. Remarkably (according to Dr. Vaidya), the visible signs of the cancer were no longer visible on the scan! This was terrific news! The treatments continued over a six-month period and January 12th, 2019, I had a third PET scan to evaluate the full results of the chemo treatments. The scan showed no "hot spots" and I was believed to be cancer free! Certainly, that is awesome!

My reason for writing and sharing this background is a concern I have over the results of the PET scan. During my first two scans, Baptist had a technology in place so they could evaluate the effectiveness of the radioactive dye injection as part of the PET scan. This was great comfort to me to be able to know the dye was injected properly and was circulated throughout my body. I knew then that the results of the PET scan could be trusted!

During my last PET scan in January, this technology was no longer being used and I was alarmed by this. What if the dye didn't fully make its way throughout my body? What if it wasn't done well? Who would know? Nobody! The results of the PET scan didn't show any "hot spots" but can I be sure there isn't some cancer remaining and growing due to a poor injection?

I have a six-month check-up coming in August 2019 and another PET scan. My hope is that this technology can and will be used for my PET scan so I can trust the results of the scan are complete and accurate. Without this technology, I don't know. I understand that the NRC does not currently require infiltrations to be reported, even if patients are being exposed to high levels of radiation that exceeds the NRC reporting limits. This policy should be changed.

I am not a doctor and am not even in the medical field. However, I do understand the need for encouraging and possibly even mandating the use of this technology for cancer patients. Why would we not want to monitor and document the success of the dye injection, which gives us the most accurate PET scan. For people like me, it is life and death.

Warm regards,
Eddie George

THELEAPFROGGROUP

August 29, 2019

Dr. Christopher Palestro:
Chairman of the Advisory Committee on the Medical Use of Isotopes
U.S. Nuclear Regulatory Commission

Dear Dr. Palestro:

On behalf of The Leapfrog Group, a national nonprofit organization representing employers and other purchasers advancing the quality and safety of American health care, I am writing in support of the NRC and ACMUI's reevaluation of NRC's 1980 determination related to infiltrations and medical event reporting [45 FR 31703].

The Leapfrog Group was founded in 2000 by large employers and other purchasers of health care, and our flagship Leapfrog Hospital Survey collects and transparently reports hospital performance, empowering purchasers to find the safest, highest quality care and giving consumers the lifesaving information they need to make informed decisions. We also assign letter grades to hospitals based on their record of patient safety, helping consumers protect themselves and their families from errors, injuries, accidents, and infections. The Leapfrog Group reports data on over 2,000 hospitals nationwide.

Diagnostic errors, such as those caused by infiltrations, are a significant concern for purchasers as well as many other stakeholders nationally. Unfortunately, data on diagnostic errors is virtually nonexistent. That is why we are interested in new data demonstrating the prevalence and consequence of infiltrations in nuclear medicine procedures. We are aware that infiltrations can have a serious impact on the quantification of a PET/CT scan, potentially affecting the care that a physician provides a patient, and can result in unnecessary radiation exposure.

In addition, we urge NRC, through this reevaluation, to ensure that patients are informed of radiological injections that result in infiltrations and that there is full public reporting of this information.

In our judgment, monitoring of nuclear medicine injection quality and reporting of infiltrations to the Nuclear Regulatory Commission would improve the quality, safety, and value of health care, and would increase transparency in our health care system.

Thank you for your attention to this matter, and please do not hesitate to contact me if you have any questions.

Sincerely

Leah Binder
President and CEO
The Leapfrog Group

DUKE UNIVERSITY MEDICAL CENTER
Department of Radiology

June 6, 2019

Dr. Christopher Palestro

Chairman of the Advisory Committee on the Medical Use of Isotopes

Nuclear Regulatory Commission

Dear Dr. Palestro,

I am a diagnostic radiologist at Duke University Medical Center, and I also have specialty certification in Nuclear Radiology (American Board of Radiology-Nuclear Radiology,1977, Cert. #20014). In my entire 40-year career in radiology I have been focused on means to improve the reproducibility of results that patients receive when they have clinical imaging studies done. From my earliest days in radiology (1978-present) I have repeatedly lectured and written that patients should get the same result if they go to the radiology department on a Wednesday than if they go on a Tuesday. Sadly, that is too often NOT the case. The reasons for this day-to-day variability are complex and reflect the use of different scanners, software, technologists, local operating procedures, and different radiologists. (As an example of my long-term interest and concern about this issue I list one of my early (1983) references at the bottom of this letter, pertaining to the variability in interpretation of lung ventilation-perfusion scans.)

One strategy to reduce variability, and a very important one, is to extract objective, reproducible, quantitative results from clinical imaging scans. Since all clinical imaging studies today are digital, this is very feasible. In 2007, with support from the Radiological Society of North America (RSNA), I left the National Cancer Institute (NIH) and formed the Quantitative Imaging Biomarkers Alliance (QIBA) [https://www.rsna.org/en/research/quantitative-imaging-biomarkers-alliance]. QIBA now has about 20 committees working on a variety of quantitative imaging biomarkers, and over 1000 participants representing more than 150 stakeholder entities and organizations. The FDA recently released a draft guidance for quantitative medical devices [https://www.fda.gov/media/123271/download] and they reference QIBA and some of our QIBA publications as the source for their definitions and concepts used in the guidance (Ref 2 below is in the Guidance).

One of our first QIBA committees dealt with the standardized uptake value (SUV) from FDG-PET scans [http://qibawiki.rsna.org/images/1/1f/QIBA_FDG-PET_Profile_v113.pdf]. Rigorous attention must be paid to all potential sources of variance in order to obtain reproducible, clinically meaningful SUV results. This is entirely possible in nuclear medicine departments that care about the quality of their results.

Because of my interest and expertise in the issues of imaging scan quality assurance and quantification, Ron Lattanze of Lucerno contacted me a couple of years ago to provide scientific consultation services to Lucerno, primarily involved in reviewing and editing their draft scientific publications. However, I have

no financial interest in the company or their products, and I am not being paid to write this letter. I attended the NRC meeting on April 3, 2019, and am writing this letter to add my perspective to the discussion that occurred at that meeting.

There is no question that reproducible, quantitative SUV results from FDG-PET scans are increasingly viewed as important in clinical oncology – both in routine clinical practice as well as in clinical trials. Here are some supporting points:

- In 2010 a colleague of mine, Tracy Jaffe, and I surveyed several hundred oncologists at NCI-funded cancer centers about tumor measurements (mostly about measurements on CT), and found that more than half of oncologists also expected SUV to be provided from FDG-PET scans (ref 3). My interactions with oncologists in many venues over the past decade indicates that the proportion who want to use SUV in patient management decisions is steadily increasing,
- In 2018 the ACR approved a quality performance measure entitled: Measure 4: Use of Quantitative Criteria for Oncologic FDG PET Imaging [https://www.acr.org/-/media/ACR/Files/Quality-Programs/Diagnostic-Imaging-2018-Measure-Set-Final.pdf?la=en], which says in part: "Final reports for FDG PET scans should include at a minimum: … d. At least one lesional SUV measurement OR diagnosis of "no disease-specific abnormal uptake". And it goes on to note: "Often injection-site infiltrates, such as arms, or attenuation-correction errors can significantly alter SUV values in lesions, leading to false conclusions." Thus, providing an accurate SUV result for ***every*** cancer patient is an expected performance measure by the American College of Radiology.
- The 2018 Guidelines of the EANM, referenced on the SNMMI web site [http://www.snmmi.org/ClinicalPractice/content.aspx?ItemNumber=6414&navItemNumber=10790#Onc], state: "Report any problems with FDG administration and image the injection area if extravasation is suspected." This acknowledges that extravasation is a problem to be avoided, but it leaves open the question as to how an extravasation would "be suspected".
- A recent example from the oncology literature concerning the increasing interest in using SUV data comes from the Eighth Edition of the Cancer Staging Manual (Ref 4), where the chapters on lung and breast cancer staging (written by oncologist expert panels) recommend that SUV values now be recorded into all cancer registries at all cancer centers:

  P. 441 (lung) "PET should provide the following information:

  a. Presence of normal or abnormal uptake in the primary tumor and quantification by maximum standardized uptake value (SUV-max).
  b. Presence of normal or abnormal uptake in hilar and mediastinal nodes and quantification by SUV-max."

  "Although SUV-max is subject to many intra- and interinstitutional variations, it is important to record it at initial staging to assess metabolic tumor response after treatment, especially after induction treatment to evaluate the possibility of tumor resection. SUV also has shown prognostic value, at least for Stage I-III squamous cell carcinoma and adenocarcinoma."

  p. p 601 (breast) - "18F-FDG-PET reports should include standardized uptake values (SUVs) of the identified lesions."

- Manufacturers are promoting the accuracy and precision of SUV from their devices, because increasingly their customers understand the value of this and expect such precision:

  [https://www.gehealthcare.com/products/molecular-imaging/discovery-mi]

  https://www.siemens-healthineers.com/en-us/molecular-imaging/xspect/syngo-via/technical-details

  https://www.usa.philips.com/healthcare/product/HC882456/ingenuity-tf-petct-system

  https://us.medical.canon/products/computed-tomography/celesteion/technology/

  All of the PET/CT scan manufacturers strongly emphasize in their marketing materials the quantitative ability of their devices, and they would not invest the engineering resources to accomplish this if they did not believe their customers wanted this level of quantitative accuracy. But obviously these devices cannot provide accurate and reproducible SUV calculation if there has been infiltration of the injection.

My comments above have been focused on the need for accurate and reproducible quantitative results in oncologic FDG-PET scans because that is my primary area of expertise. However, the literature clearly supports the need for similar reproducible quantification in several other clinical areas, such as cardiology. You have an expert from that domain and a thought leader regarding the importance of quantification on your committee - Vasken Dilsizian, M.D (Ref 5) – and he could certainly provide more context for the cardiology arena and other clinical applications. For example, a recent joint position paper from the SNMMI and ASNC on myocardial blood flow measurements (Ref 6) includes this point:

- "Consistent tracer injection profiles improve the reproducibility of MBF measurements."

Similar publications can be found recommending rigorous image acquisition parameters for PET scanning of cardiac inflammatory conditions (Ref 7), sarcoidosis (Ref 8) and many other conditions.

As discussed at the April 3, 2019 NRC meeting, infiltrated injections of FDG can also adversely affect qualitative, visual interpretations of oncologic PET studies, and I will not elaborate on that here because my professional focus has been on the need for reproducible quantitative results. Also, as stated at the April 3 meeting, and documented in the various materials provided to the committee by Lucerno, infiltrated injections are much more common in nuclear medicine than most people realize, and this is a fixable problem. The incidence of infiltrations in other aspects of healthcare delivery is much lower, and there is clear evidence that the rate of infiltrations can be significantly reduced by the standard QA methodology of documenting the occurrence and providing feedback to those responsible.

I strongly endorse the current process of having the NRC and ACMUI re-evaluate the 1980 NRC policy that states that infiltrations are virtually impossible to avoid and therefore should not be considered a misadministration or a reportable event, even if the infiltration exposed patients to radiation levels that exceed Subpart M reportable limits.

I strongly encourage the NRC and ACMUI to modify this 1980 policy and remove the infiltration reporting exemption. Such a change in policy would lead to a significant improvement in the reproducibility of SUV measurements, and greatly improve their clinical usefulness. This will translate into a major benefit to patients in this era of precision medicine.

Thank you for the opportunity to provide these thoughts and opinions,

Sincerely,

Daniel C. Sullivan, M.D.
Professor Emeritus,
Department of Radiology
Duke University Medical Center
Box 3302
Durham, NC. 27710

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Dr. Christopher Palestro
Chairman of the Advisory Committee on the Medical Use of Isotopes
Nuclear Regulatory Commission

Dear Dr Palestro,

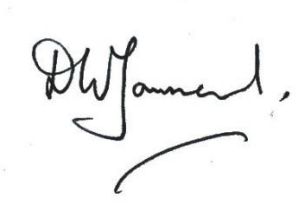
I am writing to you as co-inventor of the combined PET/CT scanner (along with Dr Ronald Nutt) that brought PET scanning into mainstream radiology for imaging oncology patients. The device became commercial in 2001 and now there are around 5000 such scanners worldwide. Over two million PET/CT scans are currently performed in the USA annually. Increasingly, PET is being used to monitor and guide therapy in cancer patients, a procedure that requires measuring the uptake of the radiopharmaceutical by the tumor. Such quantitation requires that the injection of the radiopharmaceutical be performed efficiently (without infiltration) and reproducibly.

For the last several years I have been a non-compensated scientific consultant for Lucerno Dynamics, the company that manufactures a simple device capable of monitoring the radioactive injection in PET studies. Since the device can provide a time-activity curve of the presence of the radiopharmaceutical near the injection site before the patient is imaged, it is now possible to reliably estimate the local radiation dose to the tissue in the event of an infiltration. **Given this new information I would respectfully request that infiltrated injections that exceed the reporting limit are mandated to be reported, and that the current exemption from reporting such infiltrations be removed.** While infiltrations in PET and other nuclear medicine procedures may be rare, a significant infiltration may deliver a high local radiation dose and it should be reported. Such infiltrations critically affect the integrity of the imaging study and may have consequences for the management of the patient.

As a final point, in addition to the over two million PET scans performed each year in the USA, some 40 – 45 million nuclear medicine studies are performed, also requiring a radioactive injection to the patient. Thus, even a low rate of infiltration potentially represents a radiation protection issue for a significant number of patients. The Lucerno device could also provide such a monitoring service for these nuclear medicine studies such that infiltrations which exceed the reporting limit be identified ***and reported***.

If you have any questions or require further information, please do not hesitate to contact me.

Sincerely,



David W Townsend PhD, PD, DSc, FRCR
Professor of Radiology, Fellow, IEEE

WISCONSIN COLLABORATIVE *for* HEALTHCARE QUALITY

June 12, 2019

Dr. Christopher Palestro
Chairman of the Advisory Committee on the Medical Use of Isotopes
Nuclear Regulatory Commission

Dear Dr. Palestro:

As President/CEO of the Wisconsin Collaborative for Healthcare Quality (WCHQ), I am writing with regards to the current work of the Nuclear Regulatory Commission (NRC) and Advisory Committee on the Medical Use of Isotopes (ACMUI) to evaluate the 1980 NRC policy regarding the exemption of infiltrations that exceed Subpart M reportable limits from being submitted as medical events.

By way of background, WCHQ is a nationally recognized regional health improvement collaborative devoted to performance measurement, public reporting, and quality improvement. We are a voluntary statewide consortium of healthcare organizations in Wisconsin that has led the nation in measuring and reporting the quality of care in physician groups. Our staff possess decades of experience and expertise in data architecture, performance measurement, quality improvement and practice transformation initiatives. The work of WCHQ is focused on dramatically improving the health and increasing the value of healthcare for the people of Wisconsin and given WCHQ's public reporting mission believe that performance measurement and public reporting promote greater transparency, improvement, and efficiency in healthcare.

Recently, WCHQ has become aware of the issue of nuclear medicine injection infiltrations. We have reviewed information regarding their surprising frequency and have learned that infiltrations can lead to patient harm through inaccurate diagnosis, which leads to unnecessary or inappropriate procedures. In addition to the impact on the patient, such procedures can also be viewed as contributors to healthcare waste.

We are also aware that providers do not routinely monitor nuclear medicine injections, but do monitor many other injection processes, such as chemotherapy and contrast CT injections. We know that in chemotherapy and contrast CT injections the infiltration rates are less than 1% and have been methodically studied and improved over time.

Given this, we would encourage the NRC and ACMUI to modify the 1980 policy and remove the infiltration reporting exemption. By ensuring that providers report infiltrations that exceed Subpart M limits, the NRC would increase transparency to the issue and encourage providers to improve their injection processes, which in turn will lead to improved patient care and safety.

Sincerely,

Christopher Queram
President/CEO
WCHQ

August 5, 2019

Dr. Christopher Palestro

Chairman of the Advisory Committee on the Medical Use of Isotopes

Dear Dr. Palestro,

I recently read an article, *Quality Improvement Initiatives to Assess and Improve Positron Emission Tomography/Computed Tomography Injection Infiltration Rates on Multiple Centers*. I am writing to express my concerns as this topic has significant implications for the care of the cancer patients.

As an oncologist I rely on the accuracy of the PET image at 3 critical points: 1) accurate staging of newly diagnosed cancer patient 2) response to therapy (radiation, chemotherapy or combined) and 3) continued surveillance for recurrence, post therapy. An infiltrated dose of radiopharmaceutical decreases the sensitivity of the nuclear medicine image. Significant infiltration at **any** time could negatively impact the total care and prognosis of the cancer patient. i.e. patients deemed stage I, could be more advanced stage; patients thought to be responding when they are not, because they have recurrent disease and would continue with ineffective therapy and finally "early" recurrent disease would be missed and the cycle of inaccuracies would continue.

I am aware that nuclear medicine infiltrations are currently not monitored primarily because the injection site is out of the field of view in a significant number of patients. For the reasons stated above, it is critical that every injection should be evaluated for significant infiltration and reported to the referring physician in order to increase the certainty that appropriate interpretation and measures are taken in the care of the cancer patient.

I urge the NRC and Advisory Committee on the Medical Use of Isotopes (ACMUI) to modify the 1980 policy that exempts the reporting of infiltration. This would address the concerns I have stated above. Doing so will ensure that all therapeutic decisions could be made with more confidence, knowing that the PET scan injections were done correctly and with utmost certainty. And, if a significant infiltration has occurred the oncologist and or nuclear medicine physician can be given the choice to repeat the scan.

Sincerely,

Mark Yoffe, MD

Mark Yoffe MD

Rex Hematology Oncology, UNC Health Care