UNITED STATES

NUCLEAR REGULATORY COMMISSION

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MEETING WITH THE ADVISORY COMMITTEE ON THE

MEDICAL USES OF ISOTOPES

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WEDNESDAY,

NOVEMBER 18, 2020

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The Commission met in the Commissioners' Hearing Room at the Nuclear Regulatory Commission, One White Flint North, 11555 Rockville Pike, at 10:00 a.m., Kristine L. Svinicki, Chairman, presiding.

COMMISSION MEMBERS:

KRISTINE L. SVINICKI, Chairman

JEFF BARAN, Commissioner

ANNIE CAPUTO, Commissioner

DAVID A. WRIGHT, Commissioner

CHRISTOPHER T. HANSON, Commissioner

ALSO PRESENT:

ANNETTE VIETTI-COOK, Secretary of the Commission

MARIAN ZOBLER, General Counsel

ACMUI MEMBERS: (attending via video conference)

DARLENE METTER, M.D., Chair, Diagnostic Radiologist

A. ROBERT SCHLEIPMAN, Ph.D., Vice-Chair

HOSSEIN JADVAR, M.D., Ph.D., Nuclear Medicine Physician

MELISSA MARTIN, Nuclear Medicine Physicist

MICHAEL SHEETZ, Radiation Safety Officer

P R O C E E D I N G S

10:05 a.m.

CHAIRMAN SVINICKI: Okay. I think we're ready to go in the booth. Good morning everyone. I convene the Commission's public session this morning to conduct a meeting with our Advisory Committee on the Medical Uses of Isotopes.

This is a routine meeting of our Commission to hear from this important Advisory Committee, which advises the NRC staff, not the Commission. But, I think that this, at least annual Commission engagement, is important since they are taking on a lot of very complex topics, and in some ways talking to us about things that fall more squarely in the NRC's regulatory domain, and those that have some sort of impact to the practice of medicine.

So, that is something that it is of a great utility, at least to me, and I think other members of the Commission to hear from medical practitioners and other specialists on these complex topics.

So again, I will recognize each speaker that we hear from, from the Advisory Committee. And then after that, Commissioners will be recognized for a round of questions.

But, before we get started, would any member of the Commission like to make any opening remarks?

(No response)

CHAIRMAN SVINICKI: Okay. Hearing none, then we will begin with the current ACMUI Chair, Dr. Metter.

And Dr. Metter will be giving us an overview of ACMUI activities. And so the booth will now pull up the remote feed of Dr. Metter.

DR. METTER: Good morning Chairman Svinicki and Commissioners Baran, Caputo, Wright, and Hanson. I'm Darlene Metter, the ACMUI Chair and Diagnostic Radiologist.

Thank you for taking the time to meet with representative members of the ACMUI, who will be reporting on certain major issues addressed by the Committee in 2019 and 2020.

As the ACMUI Chair, I will be presenting an overview of the 2019/2020 ACMUI activities. Are my slides up?

CHAIRMAN SVINICKI: Yes. Your slides are viewable here in the room. I think remotely as well.

DR. METTER: Okay. Next slide, please. I really don't have a remote view of the slides that are being presented.

But, today's Agenda, Dr. Robert Schleipman will follow me as the ACMUI Vice Chair. And he will be presenting the ACMUI comments on the staff's evaluation of training and experience for radiopharmaceuticals requiring a written directive.

Ms. Melissa Martin is our ACMUI Nuclear Medicine Medical Physicist. And she will be presenting the ACMUI comments on extravasations. Next slide.

Following Ms. Martin is Mr. Michael Sheetz, our ACMUI Radiation Safety Officer. And he will be presenting his comments on patient intervention and other actions exclusive of medical events.

Following Mr. Sheetz will be our Nuclear Medicine Physician, Dr. Hossein Jadvar, who is presenting a very interesting topic on trending radiopharmaceuticals. Next slide.

So, my presentation as Chairman Svinicki stated, will be an overview of the ACMUI activities. The format will be reviewing the role of the ACMUI; looking at the current membership of the ACMUI; review the many topics presented at the ACMUI meetings in 2019 and 2020.

We'll look at the current subcommittees. And lastly, I'll give a final comment about the future. Next slide.

So, the role of the ACMUI is to advise the U.S. NRC staff on policies and technical issues that arise in the regulation of the medical use of radioactive material in diagnosis and therapy.

The ACMUI at times is also asked to comment on changes to NRC regulations and guidance. And to evaluate certain non-routine uses of radioactive material. Next slide.

Furthermore, the role of the ACMUI also is to provide technical assistance in licensing, inspection, and enforcement cases. And to bring key issues to the attention of the Commission for appropriate action. Next slide.

The current ACMUI membership consists of 12 members. The Healthcare Administrator is Dr. Arthur Schleipman. Our Nuclear Medicine Physician is Dr. Hossein Jadvar.

We have two Radiation Oncologists, Dr. Ronald Ennis and Dr. Harvey Wolkov. Our Nuclear Cardiologist is Dr. Vasken Dilsizian.

I am the Diagnostic Radiologist, Dr. Darlene Metter. And our Nuclear Pharmacist is Mr. Richard Green. Next slide.

The ACMUI membership also consists of two Medical Physicists, with a specialty in Nuclear Medicine, is Ms. Melissa Martin, a

specialty in Radiation Therapy, is Mr. Zoubir Ouhib.

Our Radiation Safety Officer is Mr. Michael Sheetz. Our Patient's Rights Advocate was Mr. Gary Bloom, but he recently resigned from the ACMUI and the NRC staff is currently addressing this vacancy.

Our FDA Representative is Dr. Michael O'Hara. And our Agreement State Representative is Ms. Megan Shober. Next slide.

There are many ACMUI topics presented at the ACMUI meeting in 2019 and 2020. These include training and experience requirements for all modalities; training and experience requirements for administration of radiopharmaceuticals requiring a written directive; Y-90 microspheres brachytherapy licensing guidance; Germanium-68/Gallium-68 pharmacy grade generator licensing guidance. Next slide.

Other topics included Xcision GammaPod licensing guidance; evaluation of infiltrations and extravasations; Regulatory Guide 8.39, Release of Patients Administered Radioactive Material, Revision 1, Phase 1; an analysis of the 2018 medical events and appropriateness of medical events reporting; and a very interesting topic on status of emerging technologies licensed under 10 CFR 35.1000. Next slide.

Other topics addressed in the 2019 and 2020 ACMUI meetings were U.S. Pharmacopeia General Chapter 825. A very interesting presentation was made on trends in radiopharmaceuticals.

And because of the COVID pandemic, the NRC and ACMUI created a subcommittee with recommendations for NRC COVID-19 regulatory relief options.

We have several ACMUI subcommittees, and they reported

during these meetings on the Interventional Radiologists, bylaws, institutional memory, and there was a discussion on external communications with the ACMUI with other professional societies. Next slide.

During the 2019/2020 ACMUI meetings, we had eight staff presentations. These include summary of changes of 10 CFR Part 35, medical events update; medical event abnormal occurrence criteria; the NRC staff evaluation of training and experience requirements; past ACMUI recommendations and NRC response; NRC regulatory process and other tools; ACMUI reporting structure, membership composition and balance; and an NMED overview. Next slide.

There are nine current ACMUI Subcommittees. These include Training and Experience for all Modalities, infiltrations and extravasations, medical events, bylaws, institutional memory, patient intervention, the interventional radiologist, the COVID-19 impact on the medical community, and abnormal occurrence. Next slide.

So what about the future? Well, the ACMUI will continue to provide assistance to the NRC staff in providing advice and technical assistance; comment on NRC regulations and guidance as requested; evaluate uses of radioactive material; and bring key issues to the attention of the Commission. Next slide.

And these are my acronyms. Thank you for your attention. This concludes my presentation. And I thank you for your attention.

I turn it back to Dr. -- Chairman Svinicki.

CHAIRMAN SVINICKI: Thank you very much Dr. Metter for that overview. Next, the Commission will hear from Dr. Robert Schleipman,

who is the current Committee Vice Chair, on the topic of ACMUI's comments on the staff's evaluation of training and experience requirements for radiopharmaceuticals requiring a directive.

Dr. Schleipman, please proceed.

DR. SCHLEIPMAN: Good morning. I was invited, as you said, to discuss the ACMUI T&E's Subcommittee's report, in which we evaluated the NRC staff presented draft paper for with options for T&E requirements.

Admittedly, much has transpired since then, including a rule making proposal from NRC staff to the Commission, which I would also like to briefly address. Next slide, please.

At the time of this report, our members included the following, since then Dr. Hossein Jadvar has joined the Subcommittee, and Mr. Gary Bloom very recently left the ACMUI. Next slide.

As you know, NRC staff were asked to consider the following: whether it made sense to establish tailored T&E requirements for different categories of radiopharmaceuticals, how those categories might be determined, what would be the appropriate T&E requirements for each category, and whether those should be based on hours of T&E, or focused more on competency. Next slide.

So, we reported on the draft paper in October of last year. Next slide, please.

Several points stood out in the draft's report, the staff's draft report. Number one that access issues maybe somewhat outside the scope of NRC regulations. And two, the likely complexity of emerging therapeutic

radiopharmaceuticals. Next slide.

The staff envisioned two regulatory approaches. The first, removing prescriptive NRC requirements and review, represents a significant departure from past and current practice. Next slide.

This new framework included multiple options. The first proposed that physicians could be certified by any specialty board.

The Subcommittee cautioned that this would require other boards to locate, provide, and develop expertise for curriculum and training programs. Next slide.

And that this approach presented a potential for dilution of T&E requirements. Furthermore, the alternate pathway was not addressed there. Next slide.

The next option proposed that licensees would develop their own process for determining adequacy of T&E. This would likely introduce widely disparate criteria, did not address -- next slide, please.

Did not address transfer of the AU to other locations, nor how this might be operationalized in smaller institutions with fewer resources. Next slide.

The next option reflects the first, refines the first rather. And that other specialty boards could confer AU status, but with a caveat that those boards would be recognized by the NRC.

The Subcommittee again expressed concern that appropriate comprehensive training and experience would need to be realized and affirmed. This option also removed the alternate pathway, which potentially could adversely impact access to procedures. Next slide.

Now, turning to the second regulatory framework, essentially the prescriptive options. The Subcommittee, and I would add, many key stakeholders, endorsed the status quo.

That was established on the record of safety under these requirements, as well as the familiarity of these by training programs, regulators, and inspectors. Furthermore, clinician members of the Subcommittee also saw no intrusion on their scope of practice from these regulations. Next slide.

The proposal to tailor T&E requirements to specific categories of radiopharmaceuticals was not endorsed by the Subcommittee.

Members pointed out that unit dose delivery does not remove many safety concerns such as spills, infusion errors, patient events, all of which would require expertise in dosimetry, radiation protection, and risk mitigation. Next slide.

Tailored requirements not for each category, but rather for every radio -- new radiopharmaceutical was also deemed inadequate by the Subcommittee. Next slide.

They felt that this would delay introduction of new therapies, and require multiple reauthorization of authorized users. Next slide.

Finally, a team-based partnership approach was proposed, also deemed problematic as it potentially relocates, if you will, the comprehensive expertise requirements away from the authorized user to others. Next slide.

And while less prevalent than in years past, hierarchies still exist in the hospital setting, with asymmetric scopes of practice and authority,

which may make safety calls by subordinates more difficult.

So, I'm going to skip, if you don't mind, the next several slides, because they just repeat what I just said. I think we need to land on slide 35.

Our Subcommittee recommendations were to maintain the status quo under 10 CFR 35.390. But we did recognize that specific requirements could be critically reassessed. Particularly the requirement of 700 hours for training. Next slide, please.

There was one minority opinion, which recommended a hybrid approach that did not list the authorized user on the license. Next slide.

So, the next several slides discuss recent factors related to training and evaluation. I will caution that these were not discussed by the convened Subcommittee.

So, as you know, in January of this year, NRC staff submitted a rule making plan for training and experience requirements similar to the draft report the Subcommittee evaluated.

The rule making plan considered vary options -- varied options for T&E, ranging from retention of the status quo, tailored T&E requirements by specific classes of radiopharmaceuticals, and so forth.

Staff ended up landing on, and endorsed Option 3. Whereas a performance-based approach would remove, review and approval of T&E for authorized users by the NRC and Agreement States.

And would instead recognize certification by a medical specialty board recognized by the NRC or an Agreement State. Next slide.

Again, we have not, as a Subcommittee nor ACMUI, formally

reviewed this proposal. Though I point out that Option 3 within the rule making proposal is quite congruent with Option 1c of the previously discussed draft paper.

We did not endorse this. We endorsed the status quo. However, we did state that Option 1c might be feasible if, and only if, the appropriate level of training and experiences required, and that the NRC would apply sufficient rigor in evaluating radiation related content and competencies as we discussed.

Furthermore, Option 1c did not provide an alternate pathway, which we do recognize as being a flexible and valuable addition. Next slide, please.

As you know, there was a public broadcast by the Commissioners in January of this year. Among other items, the staff's rule making proposal was discussed.

And some insightful comments and related questions followed that discussion, such as what sort of access issues might occur with the removal of the alternate pathway?

A question of, what if no new boards would be developed by other specialties either through not having enough expertise, or the prohibitive cost involved in this?

What sort of post-board certification competency requirements might be needed? And then also, is there a way to move forward in the regulations without listing the authorized user on the license? Next slide.

Then as evidenced by our remote meeting, the novel Corona virus pandemic continues to disrupt and alter the landscape, especially the

healthcare delivery and education workspace.

Several NRC authorized specialty boards have adjusted their experiential requirements, here from the American Board of Nuclear Medicine. Next slide, please.

The ABR as well, American Board of Radiology. Though they did stress that the accreditation council for graduate medical education has made it clear that case log numbers are suggested targets and not absolute requirements.

And that the attestation of clinical competency was in, was the major milestone needed. Next slide, please.

Similarly, they regulate medical physics education programs. And said the same thing. Next slide.

The American Board of Radiology also noted that either they nor the ACGME had authority to waive any NRC requirements for training. Next slide.

In addressing COVID-19 precautions, the NRC has been proactive in issuing temporary regulatory relief. Unfortunately, I couldn't hear yesterday's presentation.

But, until these slides -- up until these slides were made, these initiatives had not specifically revised T&E requirements.

I would say that some pandemic era change, such as remote learning and remote working, will likely persist for economic and logistical reasons in the post-recovery phase.

And there may be an opportunity through the regulations or rule making to incorporate some of these into T&E requirements. Next slide.

So, in conclusion, the Subcommittee looks forward to not so much continue its review, but returning to its review. Which may be a more apt description, as we have held off following and waiting for sort of a signal of where the NRC is headed from a regulatory approach of T&E requirements.

So, I thank you very much for this opportunity. And I look forward to our discussions this day.

I would like too next send it back to Chairman Svinicki.

CHAIRMAN SVINICKI: Thank you very much, Dr. Schleipman. For our next presentation, we will hear from Ms. Melissa Martin, who is the ACMUI Nuclear Medicine Physicist representative on the topic of ACMUI's comments on extravasations.

Ms. Martin?

MS. MARTIN: Thank you very much, Chairman Svinicki and other Commissioners. I'd like to give a report of our Subcom -- the ACMUI Subcommittee on the evaluation of extravasations. Next slide, please.

I have no financial disclosures. Our Subcommittee members consisted of Dr. Dilsizian, Mr. Richard Green, myself as Chairman, Mr. Michael Sheetz, Ms. Megan Shober, and at the time, our patient advocate, Laura Weil. Our resources from the NRC were Maryann Ayoade and Said Daibes.

What our Subcommittee charge was, was to reevaluate and provide recommendations on the NRC decision on infiltrations and extravasations, which was originally published in the Federal Register in 1980.

The purpose of the Subcommittee -- oh, next slide, please. The purpose of the Subcommittee was to evaluate and review the NRC's current decision on infiltrations and extravasations when radionuclides are

injected into patients. Next slide, please.

The criteria for misadministration from the 1980 Federal Register consisted of basically the following: either the administration of the wrong source, the wrong patient, the wrong route of administration, diagnostic doses differing by more than 50 percent from the prescription, or therapeutic doses differing by more than 10 percent from the prescription. Next slide, please.

There was an exclusion of extravasation from the misadministration definition. And this was as follows: extravasation is the infiltration of injected fluid into the tissue surrounding a vein or artery.

Extravasation frequently occurs in otherwise normal intravenous or intra-arterial injections. It is virtually impossible to avoid.

And therefore, the Commission does not consider extravasation to be a misadministration. This was from the 1980 decision. Next slide, please.

In 2002, the definition was changed. Basically we went from calling a misadministration to defining a medical event.

And the medical event is defined as a discrepancy of a total dosage of plus or minus 20 percent of the delivered dose. Next slide, please.

The prior discussions of extravasations of radiopharmaceuticals consisted of a reconsideration of the -- by the ACMUI at both the December 2008 and the May 2009 meetings.

Decisions at both of these meetings were that extravasation of radiopharmaceuticals not be considered to be a medical event at that time.

The tech -- in April 2019, the ACMUI was presented with a

technology that identifies the following: extravasations of PET radiopharmaceutical injection sites early in the process, and the effect on the SUV or Standardized Uptake Value of tumors or organs when extravasation occurs. Next slide, please.

The clinical evaluations of extravasation. The main point of discussion of extravasation of radiopharmaceuticals is that the denominator for this problem is several million injections per year of all radiopharmaceuticals injected.

Extravasation problems are not limited to PET isotopes only. Prevention of extravasation is a medical training issue for the authorized user physician and the technologist under the supervision of the AU, which is considered medical practice. Next slide, please.

So, relative to the SUV of the F-18 PET isotopes. Currently, there are 48 radiopharmaceuticals approved by the FDA, including five IV therapeutic drugs.

Extravasation of the six fluorinated compounds, including the F-18 PET drugs, can bring about discrepancies in the SUV. That is true.

We are all very aware of that. SUV value is not relied on solely by the physician making the decision as to whether the study was adequate.

What about isotopes other than F-18? Next -- this is the next slide, sorry. For isotopes other the FDG isotopes, which are used for the PET scans, it is difficult to quantify non-F-18 drugs left at the injection site. And difficult to assign the radiation dosage attributable to it.

When extravasation of radiopharmaceuticals occurs, there is

a variable delay in the biodistribution of the isotope after injection. More importantly, none of the total doses in these extravasations, meet the NRC's medical event criteria.

So, what about extravasation occurrences? This Subcommittee does not consider extravasation a de facto medical event.

Extravasation frequently occurs in otherwise normal intravenous or intra-arterial injections, and is virtually impossible to avoid. Many of these patients have had lots of chemotherapy, and their veins or arteries are just not in good shape.

Not all nuclear medicine cameras in use today for PET or for SPECT can quantify the amount of radiopharmaceutical localized in the extravasation site. It is not necessarily the case that all - the extravasation sites would not necessarily be imaged during a normal procedure.

Subcommittee members are unaware of any cases of documented patient harm due to extravasation as of today.

Extravasation is a practice of medicine issue in our opinion, and not an item that needs to be regulated by the NRC. Next slide, please.

So, it is the recommendation of the Subcommittee that there is no evidence at this time for this Subcommittee to recommend a reclassification of extravasation at the injection site for radiopharmaceuticals to be considered as a medical event.

This Subcommittee recommends that extravasations that lead to unintended permanent function damage be reportable as a medical event under 10 CFR 35.3045(b). Next slide, please.

This Subcommittee recommends that extravasations be

considered a type of passive patient intervention similar to the recommendations from the ACMUI Subcommittee, which was presented during the ACMUI public meeting in October 2015, and referenced in the Patient Intervention Subcommittee report dated April 2017.

And should be captured in the NRC's current definition of patient intervention under 10 CFR 35.2. Next slide, please.

We did have one member of the Committee what wanted her minority opinion expressed. And presented a different perspective on potential medical event reporting due to extravasation.

This member wanted extravasation occurrences that trigger medical event criteria of greater then 50 rem tissue dose, or less than 80 percent of the prescribed dose delivery 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 regulation. And is unwarranted. This was the minority opinion of our member. Next slide, please.

And this is the list of acronyms that I used for a reference. And I thank you very much for your present -- your opportunity to present this today.

I will now turn it back to Chairman Svinicki.

CHAIRMAN SVINICKI: Thank you very much Ms. Martin, for that presentation. The next topic will be presented by Mr. Michael Sheetz as ACMUI Radiation Safety Officer Specialist. The topic is ACMUI's comments on

patient intervention and other actions exclusive of medical events.

Mr. Sheetz, please proceed.

MR. SHEETZ: Thank you, Chairman and other Commissioners for giving me the opportunity to speak with you this morning on the ACMUI's comments on the term patient intervention and other actions exclusive of medical events reporting. Next slide, please.

These are the Subcommittee members. And the NRC staff resource. May I have the next slide, please?

So, the objective of the Subcommittee was to determine and evaluate what types of events are intended to be captured by the term patient intervention, and what should or should not be reported as a medical event.

The purpose for this stemmed from the varying views and interpretations from regulators, licensees, and previous ACMUI Subcommittee recommendations on the definition of the term patient intervention. Can I have the next slide, please?

In 2002 the regulations in 10 CFR 35 were revised to be more risk informed and performance-based, and in alignment with the revised 2000 medical use policy statement.

The term misadministration was changed to medical event. And the reporting criteria was revised to require both a type of error in the administration, and it also required exceeding a certain dose threshold.

The errors are wrong dose, wrong radioactive drug, wrong route of administration, wrong patient, wrong mode of treatment, or wrong treatment site. And the dose threshold was set at 50 millisieverts effective dose equivalent of 500 millisieverts to an organ or tissue.

It was again stated at that time that the purpose of reporting medical events was one, for the NRC to evaluate if there was a breakdown in the licensee's program for ensuring the byproduct materials administered had corrected by the authorized user. And also to evaluate the corrective action taken by the licensee to minimize the chance for recurrence.

And two, if there was a generic issue that should be reported to other licensees so that they could take appropriate action, and thereby reduce the likelihood of other similar medical events. May I have the next slide, please?

It is interesting to note that there were several specific exclusions to medical event reporting. As we heard in the previous presentation by Ms. Martin, in the 1980 final rule, the NRC specifically excluded extravasation as a misadministration.

There are also two specific exclusions to medical event reporting in the 2002 rule. One is for permanent implant brachytherapy or sources that were implanted in the correct site but migrated outside the treatment site.

And the other is when an event that resulted from patient intervention, where patient intervention was defined as, and I quote, actions by the patient, whether intentional or unintentional, such as the lodge -- dislodging or removing treatment devices or prematurely terminating the administration, end quote.

It should be noted that in the 2018 amended Part 35 Regulations for the reporting and notification requirements for medical event, no changes were made to the extravasation for patient intervention exclusions.

And the next slide, please.

There are also several patient specific events incorporated in Part 35.1000 licensing guidance, which are exempt from the medical event reporting requirement.

In the Radioactive Seeds Localization Licensing Guidance, there's an exemption for medical reporting for cases either the patient failing to return for those scheduled explant surgery, and a physician determination not to explant the seed due to various patient conditions, where doing so would jeopardize the patient's well being.

Here various patient condition is intended to address situations where either the implanted seed may have migrated close to sensitive nerves or vessels, where surgical removal may cause significant patient harm.

Or the patient's medical condition has changed such that the patient maybe at the high risk to physically tolerate the surgical explant procedure.

In the Y-90 Microsphere Licensing Guidance, there's an exemption for medical event reporting if the procedure must be modified due to emergent patient conditions that prevent administration in accordance with the written directive, such as arterial spasm or sudden changes in blood pressure.

There is also an exemption if the total administered activity was less than that prescribed due to stasis, or if a dose to the wrong treatment site is due to shunting, concerning the evaluated part of the treatment in accordance with the manufacturer's procedures.

All of these exemptions are intended to address an

anatomical or a physiological condition of the patient that may have affected the administration or of the therapy in accordance with the written directives. And are out of the control of the AU or licensee.

These types of events are purposely excluded from the medical event reporting requirement, because they cannot be completely controlled in following the categories of the practice of medicine. May I have the next slide, please?

So, at issue is what type of events are intended to be captured by the term patient intervention? And what should or should not be considered a medical event?

As noted by the definition of patient intervention, it was intended to address physical action taken by the patient, intentional or unintentional, which caused a deviation in the administration of byproduct material from that which was directed by the AU.

It is also assumed that the licensee did everything it could to prevent patient intervention during the treatment. And that the actions taken by the patient were practically out of the licensee's control.

For example, a patient pulls out an applicator during an HTR treatment, or a patient refuses completion of the prescribed treatment, these would be considered intentional or voluntary physical actions taken by the patient.

However, there could be a situation where the patient's anatomy or physiology -- physiological condition contributes to, or causes a deviation in administration of byproduct material from that which was prescribed by the AU, such as extravasation, migration of implanted radioactive seeds,

arterial spasms or shunting with Y-90 Microspheres.

Or for example, a patient experiences a cardiac erythema halfway through a gamma knife treatment, requiring urgent medical care, thus preventing the completion of the treatment. These would be considered unintentional or involuntary actions taken by the patient.

In all of these cases, the patient caused the deviation from the prescribed treatment which would meet the medical event reporting criteria. And in all of these cases, the events could not have been reasonably prevented by the licensee.

Therefore, it would seem reasonable for both types of examples, intentional or voluntary actions, or unintentional or involuntary actions, to be considered a type of patient intervention.

A reportable medical event is meant to be an event that occurred due to some treatment error on the part of the licensee. If the medical event criteria are met due to a patient death, patient choice, or because of a changing medical condition was out of the control of the licensee, it should not be reportable as a medical event.

The value of recording such unavoidable patient medical specific events is questionable, since it will not help to prevent such events in the future. May I have the next slide, please?

So, since extravasation is currently an issue of the petition of proposed rule-making and both the ACMUI Extravasation and Patient Intervention Subcommittee had made recommendations to classify extravasations a type of patient intervention, I thought that I would try to dive a little deeper into the rationale for this position.

Performing an intravenous injection requires a certain technical skill to locate and position the needle in the vein to infuse the radiopharmaceutical. However, even the most skilled individual will occasionally not take the needle far enough into the vein, have the vein roll off to the side, or push the needle through the vein, resulting in some leakage of the radiopharmaceutical into the surrounding tissue during the injection.

Patient anatomy also plays a large part in obtaining a successful injection. Factors such as age, body habit, hydration and prior chemotherapy can all affect the ability to obtain a complete injection without any leakage or tear in the vein wall.

So, a successful injection is dependent on a combination of the required technical skills, and the ability to navigate the patient's anatomical landscape.

Studies have shown that extravasations occur anywhere from a faction to several percent. Studies have also shown that it is very rare for an extravasation to cause any type of patient harm or tissue damage.

Those that do, are mostly from therapeutic radiopharmaceutical administrations. Because of all these factors, the performance of an injection of a radiopharmaceutical, is truly a medical practice issue.

While there should be a quality assurance initiative to monitor and improve extravasation rates at an institution, this should be conducted as part of medical practice, and not something that is regulated. Next slide, please.

The following are the ACMUI Subcommittee positions on

medical events and patient intervention. The purpose of the medical event reporting rules to evaluate if there was an error or problem in the licensee's program for ensuring the byproduct material or radiation from byproduct material was administered as directed by the AU.

Or, if there was a generic issue, this should be reported to other licensees, thereby reducing the likelihood of other medical events.

If an unanticipated event occurs during a properly performed clinical procedure, and results from actions taken by the patient which could not have been reasonably prevented by the licensee, or from the anatomical or physiological condition of the patient, which falls in the realm of medical practice, then it should not need to be reported as a medical event.

Reporting such unavoidable patient specific medical events will not help to prevent such events in the future. And doing so could potentially infringe on the practice of medicine. May I have the next slide, please?

So, the ACMUI recommendations are, the current definition on patient intervention in 10 CFR 35.2 should be interpreted to include both intentional or voluntary actions taken by the patient, such as removing an implanted brachytherapy source applicator, or refusing to continue in the prescribed course of treatment.

And also, unintentional or involuntary actions, which would include medical outcomes resulting from anatomical or physiological conditions of the patient such as extravasation, migration of implanted radioactive seeds, arterial spasms, and the onset of other underlying medical diseases and disorders which interfere with the prescribed treatment.

This expansion of the term patient intervention is consistent

with the original definition which was developed in 2002.

This Subcommittee agrees that medical events resulting from patient intervention should not need to be reported as it would potentially infringe in the practice of medicine. And it will not help to prevent such events in the future.

Medical events resulting from patient intervention in which the administration of byproduct material or radiation from byproduct material results or will result in unintended permanent functional damage to an organ or tissue or a physiological system as determined by a physician, should be reported as required by 10 CFR 35.3045(b). Next slide, please.

And my acronyms. And that concludes my presentation. And I return it to the Chairman.

CHAIRMAN SVINICKI: Thank you very much, Mr. Sheetz. The next presentation will be from Dr. Hossein Jadvar in the capacity of the ACMUI nuclear medicine physician specialty. The top is the ACMUI presentation on trending radiopharmaceuticals.

Dr. Jadvar, please proceed.

DR. JADVAR: Thank you, Chairman, and Commissioners. Good morning. I'm delighted to be meeting you all virtually.

I would mention my topic is on trending radiopharmaceuticals.

Can I have the next slide, please? Please note that all the agents that I will cover in this presentation are investigational and not currently approved for clinical use.

Next slide, please? This is my outline. I'm going to talk about

some of the recent radiopharmaceutical approvals and then I'll focus on oncologic and theranostic agents. And I will define theranostic in one of my upcoming slides. And then I end with a summary.

Can I have the next slide, please? So there has been what can be considered a renaissance with regard to activity in approval of radiopharmaceuticals, particularly in positron emission tomography, or PET. As you can see, in 2012 through 2014 we had three radiopharmaceuticals that were approved under neuropsychiatric domain for imaging evaluation of patients with cognitive impairment and dementia, particularly Alzheimer's disease.

More recently, in 2019 there was another radiopharmaceutical, fluorine-18, fluorodopa, that was approved by the FDA for imaging evaluation of patients with movement disorders including Parkinson's syndrome.

And very recently, just several months ago, a few months ago there was a radiotracer that was approved called flortaucipir for imaging evaluation of the tau deposits, which is a pathology in the brain of patients with Alzheimer's disease.

Under the cancer domain or oncology, back in 2012 there was a tracer, C-11 choline that was approved for imaging evaluation of patients with biochemical recurrence of prostate cancer after definitive primary treatment. It was followed by the very first alpha particle radiotherapeutic, radium-223 dichloride in treatment of patients with metastatic castration-resistant prostate cancer. This was first-in-class approval for alpha particle therapy.

This was soon followed in 2016 with a tracer for -- with a name of fluciclovine for imaging evaluation of patients with biochemical recurrence of prostate cancer, and two agents, one for imaging; one for treatment of patients with neuroendocrine tumors. And those are the gallium-68 dotatate and lutetium-117 dotatate, which is a beta particle.

And very recently, in 2020 there was a copper-64, a longer half-life, 12-hour half-life dotatate agent for neuroendocrine tumor imaging. And also very recently the last approval was fluoroestradiol, which is a PET tracer that targets estrogen receptor in patients with recurrent breast cancer.

May I have the next slide, please? So this is just to show you the concept of the theranostics. Basically we have a target. This is a biological target. It could be antigens, receptors, enzymes or transporters. And then the idea is to design an agent that has affinity for these targets. This could be antibodies, it could be peptides or other agents that have that affinity for that particular target. And then those are linked to an isotope. Now the isotope could be a reporting unit, which is for imaging. And you see some examples under that. Or it could be cytotoxic, where you can deliver to that target beta or alpha particles for very localized radiation treatment of that area that this agent is actuating.

And the idea here is, which is consistent with what's called a precision medicine or individualized care, is to target tumors that overexpress these targets for localized treatment and less toxicity. So this called a theranostic concept.

Next slide, please? I just want to go over some examples of tracers that are not approved but are being studied in clinical trials. This is one

of them. It's the zirconium-89 trastuzumab. This is targeted to the human epidermal growth factor receptor 2, or HER2, which is an important target in patients with breast cancer.

This image is a PET image of this particular PET tracer just to show you that if the patient -- for example, in this case a woman with breast cancer. If the primary tumor is not expressing the HER2, there are sites of the tumor and metastases may actually express the HER2 receptor. So therefore one cannot decide on not using an appropriate drug, in this case Herceptin, or trastuzumab, just based on the histology information from the primary tumor.

Cancer is very heterogeneous and therefore with tools like this we can actually see if there are other sites of this disease in this patient that may be expressing in this target and therefore the patient may be a candidate for that particular drug.

Next slide, please? This is another very exciting development for an anti-CD8 minibody. There is a lot of activity going on in the cancer immunotherapy domain basically using the patient's own immune system to fight cancer. But to do that the tumors need to have a sufficient number of inflammatory cells. In this case cytotoxic T cells that express CD8. And to find out or decide which one of these patients with cancer would be a good candidate for various types of cancer therapy drugs, this type of PET imaging with this type of tracer would be very important.

Next slide, please? This is another very exciting development. This is called gallium-68 FAPI, which stands for fibroblast activation protein inhibitor. This particular radiotracer was designed in Heidelberg, Germany and has a bright future I think for theranostics, not only

for imaging cancer, but also to use it for treatment of cancer.

The idea here is that we are not imaging the tumor directly as we do with FDG, which is the most common PET radiotracer, but what we are imaging is actually the microenvironment of the tumor. And you can see in these particular images that I show here, these are PET scans in various types of cancers. There are situations where the primary tumor or the tumor sites may not be very FDG-avid particularly, but the microenvironment of the tumor actually shows a high signal and therefore we can not only have a good idea of the extent of the tumor, but also fight cancer on both grounds, both targeting the tumor itself, but also targeting the microenvironment of the tumor for synergistic effect and better patient outcome.

Next slide, please? This is another area which is rapidly developing and very exciting. This is based on prostate-specific membrane antigen, or PSMA, which is being explored in patients with prostate cancer, although it is not specific to the prostate and it is not specific to cancer. The name is a rather misnomer, but it is basically an enzyme which is a transmembrane enzyme and it's overexpressed in a tumor, especially in prostate cancer, but also in other tumors. And therefore this is a very good target for not only imaging prostate cancer, but also for delivering treatment.

Next slide, please? So this shows you just three of the PET radiotracers that have been designed for targeting the PSMA. The first one, gallium-68 PSMA-11 is the oldest one, or the grandfather of all of them. And that was designed in Heidelberg, Germany. And a number of radiopharmaceutical companies are in process of hopefully getting that FDA-approved and available to the clinics soon.

The second is F-18 with a longer half-life. And that was spearheaded from Johns Hopkins University investigators.

And the last one that I showed here in this slide is another F-18 labeled PET radiotracer targeting PSMA, which is called PSMA-1007. And that is -- also was designed in Heidelberg, Germany, and is being studied.

Next slide, please? Just to show you some of the exciting work that has been done in this domain. This is an article that was published last year in *Lancet Oncology*. This compared the gallium-68 PSMA-11 PET/CT with Fluciclovine, which is a currently FDA-approved PET agent that I mentioned in my earlier slide, to show that this particular target, PSMA, and this tracer, gallium-68 PSMA-11, is substantially more sensitive in detecting a small site of disease. These are in patient with very low PSA levels where it's very clinically relevant to see if there any sites of disease. So that if the patient has metastatic disease, they can be a candidate for systemic therapy. If there is localized disease, they can be a candidate for salvage radiotherapy.

Next slide, please? This also was shown to -- this study was also very nice to show that we are missing a lot of sites of disease with PSMA-11 PET/CT in these patients who were being considered for salvage radiotherapy, basically just treatment to the prostate bed after radical prostatectomy their PSMA-11 showed that there are many, many other sites that we are kind of blinded to and don't know about.

This image that you see on the right-hand side -- the green area is an area that would have been treated with radiotherapy, but all the yellow dots are the areas of the disease that would have been missed in this treatment domain, and therefore the patient would have stayed that type of

treatment. So basically showing you the substantial amount of information that we can get from this type of tracers.

Next slide, please? And based on that very exciting result there is currently a clinical trial going on on PSMA called PSMA-SRT trial in patients with -- after radical prostatectomy who are presenting with biochemical recurrence. And the idea is to see if PSMA tests -- if it's incorporated into care of these patients, if it decreases the salvage radiotherapy failure at five years in comparison to the clinical arm where gallium-67 PSMA-11 is not used. Next slide, please? Then I mentioned the theranostics and I talked about the PSMA-based imaging, but when you image the target and you see the targets available, you can actually have exactly -- or essentially very similar molecules and deliver localized radiation. In this case with lutetium-177, which is a beta emitter, with PSMA is being delivered in this patient. You see on the left-hand side PET images of a man with very diffused widespread metastatic disease in his bones and many other sites and who is being treated with lutetium-177 PSMA-617. And as we go after four -- as you see after four cycles of the treatment he does pretty well. And the imaging looks much, much better with a decline of PSA from almost a level of 1,000, as you can see on the right panel or the graph -- it's going down from 1,000 to almost near zero. And by the way, these studies have been done in patients who basically have exhausted all types of conventional treatment. And even in this very difficult case there is a very good response, or remarkable responses in some patients.

Next slide, please? And this was -- these encouraging results was looked by a phase 2 study in Australia that was published in *Lancet Oncology* 2018. And in this, 30 men with metastatic castration-resistant

prostate cancer it was shown that lutetium-177 PSMA-617 is actually quite useful and can decrease the PSA substantially in a large number of patients.

Next slide, please? And there are a number of clinical trials going on right now with lutetium-177 PSMA. One of them is VISION trial, which has already completed. It compares the PSMA treatment versus the supportive care. This is very much patterned after a single clinical trial that ended up having the radium-223 dichloride to be approved and we are awaiting for the results of the VISION trial.

Next slide? Another exciting trial is the TheraP trial which compares the lutetium-177 PSMA versus a currently approved -- FDA-approved chemotherapy, cabzitaxel, in patients with metastatic prostate cancer.

Next slide, please? And finally I want to mention that we are not limited only to beta particles that I showed you, lutetium-177. We can also have alpha particles. In this case you can see actinium-225 and bismuth-213 is an alpha particle agent conjugated to PSMA with remarkable responses. These images are provided here from a study that was done in South Africa.

Next slide, please? And there are other things that are coming up also. This is another alpha particle-based PSMA agent that uses thorium-227. The preclinical studies in mice have been very encouraging and that led to initiation of a phase 1 clinical trial in patients with metastatic castration-resistant prostate cancer.

Next slide, please? And finally, there are other targets that we can look at. This is another target. It's called Chemokine Receptor 4. That is overexpressed in a number of cancers. One of the exciting work that has been done was in the area of multiple myeloma. And you can see in this case

that you can use not only the CXCR4 as an imaging agent. As we can see, gallium-68 Pentixafor, but also you can conjugate it with lutetium-177 for delivering beta particle locally and treating these patients in a theranostic domain.

Next slide, please? And I mentioned that there was a dotatate agent already approved by the FDA for not only imaging but also for treatment of patients with neuroendocrine tumors using alpha particles. And just to show that there is also an -- I'm sorry, using beta particles, but right now there is also studies going on in using alpha particles for doing -- for delivering treatment to patients with neuroendocrine tumors. In this case with lead-212.

Next slide, please? So in summary I think theranostics will continue to grow with the approval and clinical introduction of many agents for targeted imaging and radioligand therapy of cancer, which fits very well with the concept of precision medicine.

Next slide? And these are the acronyms related to my slides. And thank you very much for your time and attention, and I will turn it back over to Chairman Svinicki. Thank you.

CHAIRMAN SVINICKI: Thank you very much, Dr. Jadvar. I know that while it's encouraging that there are so many promising results, that it was difficult for us to go through even some of the most promising ones in the time available, but thank you. That was very comprehensive.

And my thanks to all of the presenters from the ACMUI, but also those who supported the work of the subcommittees and the Committee overall. Again, you've laid down a number of topics that I'm certain my colleagues and I will want to pursue.

And we do rotate the order of recognition in our meetings. Today we will begin with Commissioner Baran.

COMMISSIONER BARAN: Thanks, Chairman.

Well, thank you all for your presentations. I'd like to ask some questions on the topic of whether extravasations should be reported as medical events.

The NRC is currently evaluating this issue. In 1980 the Commission established a policy that extravasation should not be considered misadministrations. This decision was based on NRC's understanding that extravasations occurred frequently in otherwise normal injections and were virtually impossible to avoid. That was 40 years ago though and obviously medical practices and technologies have advanced quite a bit.

I'll direct these questions I guess to Ms. Martin since she presented on the topic, although I know Mr. Sheetz also talked about it a little bit, but others should feel free to chime in.

What is the current understanding of how frequently extravasations occur and is there reliable data around that?

MS. MARTIN: Thank you for the opportunity to respond. One study we looked at; and actually Dr. Jadvar provided some of this data, in diagnostic administrations the percentage of extravasations was approximately 0.1 percent. And for therapeutic is about 0.2 percent. So it's not a common occurrence. It does happen.

Since 1980 patients' veins really haven't changed. So the problem of having an extravasation due to a patient having a problem with the condition of their veins, particularly if they're a chemotherapy patient, really

hasn't changed. I don't think anyone would say that extravasations are common. They do happen. They happen routinely whether it's with radiopharmaceuticals, with chemotherapy drugs, with any other type of drugs administered IV.

So we do have extravasations. Most every facility and every practitioner goes through training to try to avoid this. We have not seen a significant difference between the percent of extravasations that occur where the nuclear medicine technologist or authorized users are administering radiopharmaceuticals from anyone administering say chemotherapy drugs or administering other IVs. So it is not unique to radiopharmaceuticals that extravasations occur.

And I would certainly turn the floor over to our physicians if they would like to add anything to these comments.

DR. JADVAR: This is Dr. Hossein Jadvar. I second what Ms. Martin just mentioned. And she was referring to a study that was published in the *European Journal of Nuclear Medicine and Molecular Imaging* in 2017. It was basically a systematic review of publications on this particular topic of extravasation. And these authors basically found that 37 publications were relevant and in these 37 publications there were 3,016 cases of extravasation that folks reported. And these are all diagnostic in this group of publications.

And as Ms. Martin already mentioned the incidence of extravasation was very small, 0.1 percent. And essentially only three patients were reported to have some mild itching, or pruritus as we call it, and redness at the site of the extravasation.

With regard to therapeutic agents, which potentially could be

more problematic, there were eight publications that were looked at. And in those eight publications again the incidence was very low and none of them had permanent functional damage with regard to the patients who actually ended up having some extravasation of the radiotherapeutic drug.

But also I reemphasize, as Ms. Martin mentioned, that the extravasation is not just for radioisotopes. It can happen with chemotherapy. And so there is nothing particular to radioisotopes. Chemotherapies also are irritant and if they are deposited through extravasation, they can also cause local issues. But again, there is evidence published out there that this is not a huge or major problem. Thank you.

COMMISSIONER BARAN: Thank you. That's very helpful. And one of the other questions the NRC staff is trying to determine is whether the dose consequences of extravasations are significant. You touched on that a little bit. Is there anything else you'd want to add on the current state of knowledge on that question of the dose consequences?

MS. MARTIN: Yes, this is Melissa Martin responding from the physicists' perspective.

The actual dose calculations are fairly complicated to do an accurate dose assessment for a extravasation. Thankfully the body has a lot of physiological functions going on to clear out the extravasation, and so you have a physiological component to the calculation.

The other problem that we've run into is to try to get an estimate of the actual amount of dosage that has been extravasated. Many of the gamma cameras that are used today are of a vintage that do not give accurate uptakes. They can localize the extravasation. They can show what it

is, but they don't give you the uptake values.

And to replace that equipment you're talking a very significant amount of money to replace a camera that is perfectly functional except for the fact that it doesn't give a quantitative information on doing dose calculations. So the physicist really would not have the information needed to do an accurate calculation of the dose.

COMMISSIONER BARAN: So that's interesting. So part of what you're saying there I take it is that if we were to change the policy here and the medical event dose criterion were to apply for example of a dose to an organ or tissue that exceeds the prescribed amount by more than 50 rem, there may just be a challenge in ascertaining whether that's occurred in any particular instance?

MS. MARTIN: And the fact that basically that organ would be the skin. That's what we're looking at is the dose to the skin. That would be from an extravasation. And yes, we don't have the data right now from -- every facility that performs these examinations does not have the ability to provide the information that would be required for a nuclear medicine physicist to do a dose calculation. We could to an estimate, but it's very much of a raw estimate. It is not going to be accurate due to the limitations of the equipment that is out there.

COMMISSIONER BARAN: So at this stage would you say we have a sense, or really not, about whether or not the 50 rem dose criterion would be

met --

MS. MARTIN: No, it would be --

COMMISSIONER BARAN: -- pretty frequently or not?

MS. MARTIN: Excuse me.

COMMISSIONER BARAN: No. Please go ahead.

MS. MARTIN: It would be hard to reach the 50 dose limit unless you had an extravasation of a very small area with a very high uptake. The larger the area the dose is spread out, so the actual skin dose in any one area is diminished. So the 50 rem would be -- it is possible to reach that, particularly with a therapeutic administration. It is -- again, it depends on how large an area that the radiopharmaceutical is infused into.

COMMISSIONER BARAN: Okay. And recognizing the challenges you've been discussing about making a determination on the dose, one of the things I'm trying to figure out is whether the medical event reporting exclusion for extravasations is actually impacting the amount of reporting. If we applied the medical event reporting criteria to extravasations, as ACMUI's prior patient advocate member suggested -- trying to figure out would that actually result in many extravasation-related medical events being reported if in fact it would be pretty rare that the 50 rem threshold would be met?

MS. MARTIN: In our opinion it would still be a rare event. I think Mr. Sheetz might have more information on that to help fill in that information, but we did not feel it would be a routine certainly occurrence.

MR. SHEETZ: Thank you. I'd like to comment. The challenges, as Ms. Martin alluded to, is trying to do the dosimetry calculation because of all the variables on the clearance rate of the radiopharmaceutical from the extravasated tissue the volume and shape of the extravasated tissue. And this becomes very complex. And if you consider all that, it probably clears

out and would not exceed the 50 rem tissue dose.

But if one assumes a very simply model where you assume it's one cc of the cylinder of tissue and the activity stays there until physical decay, it would only take 150 microcuries of technetium-99m or 30 microcuries of F-18 to reach the 50 rem dose. So if you do a very simplistic model, a conservative model, you will have a lot of reported medical events from this.

If you take the time to look at the clearance rate, then most likely the tissue dose would not exceed this 50 rem. So it really would create a large burden if this rule were to address extravasation as a potential medical event. Won't it would require every administration to be evaluated whether any extravasation? So that would require either an image over the site or some radiation detection system to monitor the injection site.

And then once you detect it or monitored or identified any extravasation, you would have to do the dose calculation, which would be again very complex, very time-consuming. And so yes, it would result in probably a significant number of medical event reports just because of trying to do it simplistically and not spend a lot of time on it.

COMMISSIONER BARAN: Well, this is very helpful. Thank you so much for your perspectives on this and I'm looking forward to reviewing what the staff finds and recommends this spring. Thanks.

CHAIRMAN SVINICKI: Thank you, Commissioner Baran.

Next we will recognize Commissioner Caputo.

COMMISSIONER CAPUTO: Good morning. Thank you all for coming and speaking with us this morning.

I would like to start with a few questions to Dr. Schleipman.

As I understand it there's been a misunderstanding of the NRC's training and experience proposal by some external stakeholders. I'm referring to apparently the American Medical Association has been quoted as stating that the NRC is proposing that non-physicians could become authorized users, and I think that article, quoting the AMA, was in Medpagetoday.com.

Dr. Schleipman, can you just confirm that only physicians can be qualified to be trained as authorized users?

DR. SCHLEIPMAN: Yes, that is a misunderstanding that you just mentioned.

COMMISSIONER CAPUTO: Okay. Thank you. Dr. Schleipman, again another question for you: The Certification Board of Nuclear Cardiology was established in 1996 and the NRC then recognized those physicians whose credentials had been verified by that board a few years later. Isn't the staff's current proposal to revise the training and experience regulations similar to how nuclear cardiologists became authorized in the past?

DR. SCHLEIPMAN: Can you expand that a little further?

COMMISSIONER CAPUTO: Well, it was my understanding that they were credentialed by their board prior to the establishment of our 700-hour requirement, I think.

DR. SCHLEIPMAN: I'm not sure of that. I was not a part of this group then. I do think that the nuclear cardiology -- nuclear cardiologists that I have worked with have definitely exhibited a facile understanding and training regarding radiation safety.

The NRC did recognize that board, did it not?

COMMISSIONER CAPUTO: That was my understanding, but

it also predates my own time here at the Agency.

All right. I think the issue that I wanted to highlight was just that you have on slide 36 acknowledged the training and experience requirement of 700 hours is somewhat arbitrary, so I'm just questioning whether a continuing reluctance to support a more risk-informed performance-based similar to what was used in the past with the nuclear cardiologists might be a reasonable approach considering it's been done in the past.

DR. SCHLEIPMAN: The subcommittee felt -- was concerned of dilution of training programs, but also recognized that it was hard to find a provenance of that 700 hour. That is, it was actually a greater number in years past and that it would be quite reasonable to evaluate that carefully, and as the subcommittee is willing to look at that.

COMMISSIONER CAPUTO: So given that our medical use policy statements states NRC will not intrude into medical judgments affecting patients except as necessary to provide for the radiation safety of workers and the general public, isn't it more appropriate to have physician credentialing left to the medical specialty boards such as the American Board of Internal Medicine's Oncology Board and the American Board of Urology or other expert boards within the practice of medicine?

DR. SCHLEIPMAN: The currently recognized boards: the American Board of Nuclear Medicine, the American Board of Radiology, provide those core elements of necessary training: radiobiology, shielding, dosimetry. Those are naturally imbedded in existing programs that have been approved or vetted by the NRC. So again, if a new board would be developed, they would need to have that expertise, not only to provide the training, but to assess its

effectiveness.

COMMISSIONER CAPUTO: Okay.

DR. SCHLEIPMAN: But those are medical boards, yes.

COMMISSIONER CAPUTO: Okay.

DR. SCHLEIPMAN: Are you referring to the alternate pathway?

COMMISSIONER CAPUTO: I believe so.

We have received several letters from medical oncologists that treat patients for prostate cancer who state that patients need to travel significant distances to receive their treatment. Are you familiar with any of these letters that we've received? Have they been shared with the board, or the subcommittee?

DR. SCHLEIPMAN: Oh, absolutely.

CHAIRMAN SVINICKI: Okay.

DR. SCHLEIPMAN: Absolutely. The letter from the manufacturer of radium-223, XOFIGO -- we're familiar with that -- we did note that most stakeholders felt that there were no access issues overall.

I think Dr. Metter is asking to be recognized to contribute to this, if she may.

DR. METTER: Yes. Thank you, Dr. Schleipman. I just would like to make a comment on a previous discussion point regarding the nuclear cardiologists. And the point that you did make about the training and experience of 700 hours was actually addressed many years by the cardiology training and they put the required 35.290, the Imaging Localization, as part their training requirements for their ACGME program. And so they do have that

imbedded in their training programs, because it would come to our department in nuclear medicine and we would be helping to educate them and train them for the nuclear cardiology program.

COMMISSIONER CAPUTO: So doesn't it make more sense for them to be setting the number of hours than for the NRC? Isn't there a certain argument to be made for us to defer to those boards?

DR. METTER: The thing is that I think for that, the diagnosis and imaging for the 35.290 for imaging localization is something that I think is very pertinent. And I think the current requirements are adequate for the safe use of these radiopharmaceuticals for diagnosis.

COMMISSIONER CAPUTO: Okay. I've got one last question for either of you. Has the subcommittee reached out to other boards such as the Medical Oncology Board with the American Board of Internal Medicine or the American Board of Urology to determine if they see a shortage in authorized users?

DR. SCHLEIPMAN: This is Robert Schleipman. The subcommittee has not reached out to those boards. We have seen their comments.

COMMISSIONER CAPUTO: Okay. So what is the subcommittee's basis for saying there is no shortage?

DR. SCHLEIPMAN: We raised the potential concern in an early report in February 2018. At a subsequent meeting in February 2019 after reviewing the pipeline, if you will, of training programs and certifications, we've determined that there were no objective data to confirm a shortage. We also recognize that many agreement states also made that same conclusion.

COMMISSIONER CAPUTO: Okay. One last question. I'm going to go back to what Commissioner Baran was asking about extravasations.

So, Ms. Martin, the subcommittee more or less reaffirmed that the committee does not consider extravasation to be a medical event, that it's virtually impossible to avoid, and that the subcommittee is unaware of any cases of documented patient harm. As a practice of medicine issue, the NRC need not regulate it.

However, the subcommittee recommended that extravasations that lead to, quote, unintended permanent functional damage should be reported as medical events.

If the subcommittee members are unaware of any cases of documented potential patient harm, what scenarios do you envision or have the members postulated that could cause permanent functional damage thereby requiring reporting of medical events?

MS. MARTIN: We put that in there basically to cover the potential in the future of these new drugs that are being developed.

We just don't know what would happen in the future. But if there's a possibility of one of these therapeutic agents causing a permanent damage, we are agreeable that that would be reported as a medical event.

The worst reactions we've seen to date is I think there's a few documented cases of some ulceration that have occurred. And those have been cured. They have not been permanent.

But if there is something in the future, we just wanted to make, agree that if it was a permanent damage, that should be considered a

medical event.

COMMISSIONER CAPUTO: Okay. Thank you.

MS. MARTIN: Dr. --

COMMISSIONER CAPUTO: Oh, sorry.

MS. MARTIN: Michael Sheetz has a comment if that's okay with you.

COMMISSIONER CAPUTO: Sure, absolutely.

MR. SHEETZ: Thank you. If I could just comment on that, is that if we consider extravasation a type of patient intervention, then it is consistent with the Part 35 regulations that even those events caused by patient intervention, if they result in permanent functional damage, they will be reportable as a medical event. So it's consistent with extravasation being considered a type of patient intervention. Thank you.

COMMISSIONER CAPUTO: Okay. Thank you.

CHAIRMAN SVINICKI: Thank you, Commissioner Caputo. Next we will hear from Commissioner Wright.

COMMISSIONER WRIGHT: Thank you, Chair. So good morning. I'd like to start first by just recognizing the work that you do outside of this committee as medical professionals. And I want to thank you for the sacrifices that you make each day and especially during this pandemic. You know, as a cancer survivor myself, I can personally tell you that the work that you do is very much appreciated.

And I know that your commitment to what you're doing on this committee, as well as what you're doing every day to care for your patients, keeps you up late at night, away from your family, and keeps you very busy. So

thank you for what you do.

Dr. Schleipman, as I was preparing for this meeting today, I was thinking about, again, as usual, the proposed changes to the training and experience requirements that are before us.

There's still a few issues that I'm kind of still trying to get my head around, which you summed up I think, if I remember it was like slide 41. You don't have to pull it up, but I think that was the slide.

So we've had a lot of discussion about whether there is a shortage, as Commissioner Caputo was talking about, in this country overall and in certain geographic areas.

In our SECY-20-0005, the staff recommends requiring authorized users to be certified by a medical specialty board recognized by the NRC or an agreement state and removing the alternate pathway. So I got some questions about how this may affect the number of authorized users.

My understanding is that individuals currently using the alternate pathway have a number of board certifications. Is there any indication that the boards issuing these certifications would be interested in being recognized by the NRC or an agreement state? And if not, would removing the alternate pathway close a route for certain medical professionals wishing to become authorized users?

DR. SCHLEIPMAN: Thank you, Commissioner. The subcommittee felt that it may be difficult for these boards to develop the expertise to administer training. We did not want to see the alternate pathway disappear.

Some radiation oncology and diagnostic radiology trainees

have to wait up to 15 months between completing their requirements and achieving the board certification so that granting AU status through the alternate pathway provides an additional input to the pool of authorized users and can continue to promote the access to procedures requiring an authorized user.

COMMISSIONER WRIGHT: So did I understand you to say that you did not see any issues with maybe keeping both things going, keeping the alternate pathway as well?

DR. SCHLEIPMAN: Yes, we saw value in the alternate pathway.

COMMISSIONER WRIGHT: Okay. Thank you. And I'm going to stay with you. And, obviously, anybody else can chime in if they wish.

But I want to talk a little bit about the minority opinion on T&E regarding shifting the T&E framework to focus on individuals who handle or administer radiopharmaceuticals.

So we had a commission meeting last month with OAS. And we received similar feedback, that some states feel strongly that we, at the NRC, need to shift our focus from the physicians and instead look more to those actually handling and administering the materials.

So what are your thoughts on such a shift? And I guess first would be the first question.

DR. SCHLEIPMAN: I will point out that it was a minority opinion.

I think it's, what the subcommittee had thought was that any sort of coworking, sort of team approach to administering radiopharmaceuticals

requiring a written directive would still require an authorized user understanding all of the radiation safety issues and being able to address them, particularly in the cases of infusions, infusion errors, extravasations, patient events that might occur that would require complex dosimetry and so forth, and that relegating that to others would not necessarily promote safety.

COMMISSIONER WRIGHT: So does the medical event reporting data support the assertion that authorized users are often not present or supervising at the time of these events?

DR. SCHLEIPMAN: I would defer to Ms. Martin or Mr. Sheetz on that.

MS. MARTIN: This is Melissa Martin. I would just say I've been radiation safety officer now at five major medical centers for about the past 25 years. I have never been at one of these procedures when the authorized user was not there to administer the radioactive material. It is their responsibility.

COMMISSIONER WRIGHT: Okay. Thank you. So, Ms. Martin, I'm going to stay with you --

MS. MARTIN: Uh-oh.

(Laughter.)

COMMISSIONER WRIGHT: So thank you for the presentations today from each of you. But the extravasations in patient interventions, a lot of this, especially the extravasations part, has gotten a lot of external attention.

And, you know, one thing we keep circling back to is where do we draw the line between radiation safety and the practice of medicine. So,

along those lines, I got a couple of questions. And, Michael, if you want to jump in, you can, too.

So, with the current practice and standards of care, how would a medical professional know that an extravasation happened for a diagnostic dose? And how, if at all, would that be different for a therapeutic dose?

MS. MARTIN: Well, obviously, you can, it's visual for one thing. You could also image the injection site with the camera if it was a large enough extravasation that you think it's going to affect the study that the patient is having done.

You can image it. You can document that it happened. But it's basically a visual perception.

COMMISSIONER WRIGHT: Okay. So ACMUI is proposing that extravasations be treated as a passive patient intervention.

And given current diagnostic and therapeutic doses, could you have -- and I think this piggybacks on Commissioner Caputo's question. Could you have an extravasation that met the threshold for reporting as a patient intervention and resulted in unintended permanent functional damage to an organ or a physiological system?

And I know you mentioned the new drugs, future stuff. I know you mentioned that, but under, currently.

MS. MARTIN: You can certainly reach the point of 50 rem or .5 sieverts. But what you don't reach is the level to cause permanent functional damage. That is a discrepancy. Fifty rem does not cause permanent functional damage.

Having, if you've gone through radiation oncology, you were probably given at least 180 to 200 rem or rads on a daily basis. That does not cause permanent functional damage.

So just because you reach that 50 rem dose is not going to cause you permanent functional damage. And I think we need to disassociate those two, that result from that 50 rem dose.

COMMISSIONER WRIGHT: All right. So let's stay with the 50 rem and go to less than 80 percent of the prescribed dose delivered to the patient being I guess reported as a medical event.

Can you discuss with me, maybe expand a little bit more on how a licensee would go about making that determination for an extravasation?

MS. MARTIN: Well, that's why right now that's only referred to pretty much on the PET isotopes, because the SUV values would be affected.

COMMISSIONER WRIGHT: Right.

MS. MARTIN: But what happens in most of the time is the study is repeated within a day or so. And then you start from scratch. The numbers are fine. But that number is usually picked up pretty much for the PET isotopes at this point.

I am not the physician. So certainly if Dr. Jadvar has, or Mike has other information on this, I would be glad to have them add information to that.

DR. JADVAR: Well, all I can say as a physician, you know, extravasation can occur. And as Ms. Martin already mentioned, that's usually visual. You can see that there is a little bit of, you know, a bump or swelling

maybe even forming.

And then when we do the image on the PET camera, you will see that that area is hot on the image. And, in fact, if sometimes we know for a fact that some of the tracer has been extravasated, you may want to exclude that area from image so that it doesn't damage the image processing of the rest of the scan, because it can do that.

But, you know, this comment that there is, that the, for example, warm the area, you know, using hypothermia to make sure that the clearance is made more radically. We have the patient's arm elevated. So there are interventions that we do, like massaging the area, just to make sure that the clearance is improved. And then, of course, you ask the patient if they have any symptoms of any sort in relation to that.

I have not, you know, to my experience at least, it has not been a major problem. Even the images are not that bad, you know, and then the diagnostic quality. And we are able to make our determination of what is going on with the patient.

But if there is a large amount for some reason that gets extravasated, because of the, some of these patients officially who have received many, many chemotherapies. Their veins are fragile. And that can happen. And it turns out that it may be a difficult re-do of the procedure.

We actually have, you know, our hospital and I'm sure in many other places, nurse practitioners or other folks from, typically from oncology, in our case, from our cancer center, who are very good at, you know, accessing the veins, even in these difficult cases.

So we can do that, or if nothing works, some of these patients

have what we call PICC lines or central lines. So we don't even have to worry about injecting the tracer through our own access, but the access has been provided to us. And we use that access for delivering the radio tracer.

COMMISSIONER WRIGHT: So, and one last quick question because I was -- you're hitting right where I wanted to go. So, as a patient myself, I had a port.

What is the percentage of ports for people that are getting the, you know, the real wicked stuff versus, you know, PET scans or, you know, MRIs or CAT scans or whatever? How many are going through veins versus with a port?

I would think that, I mean, just intuitively, I would think if somebody's been sick for a while, they're going to go through a PICC line or a port. Can you give me some idea what the percentage is there?

DR. JADVAR: I can't tell you the percentage. But we generally don't use the port, because that's an area that is used for delivery of chemotherapeutic drugs. And we, you know, typically we don't want to, you know, interfere with the function of that port.

But PICC lines has been used. I can't tell you the percentage for PICC lines, you know, peripherally access lines.

And again, even in patients with port and PICC lines, well, not PICC lines. PICC lines we use it. But if there is a port, there is still a way. Most of the time we are able to access the peripheral vein. And that's not a problem.

We try not to use the ports. And sometimes they tell us not to use the ports --

COMMISSIONER WRIGHT: Right.

DR. JADVAR: -- you know, the oncologists.

COMMISSIONER WRIGHT: Thank you so much. All right.

CHAIRMAN SVINICKI: Thank you, Commissioner Wright. Next we will hear from Commissioner Hanson.

COMMISSIONER HANSON: Thank you, Chairman Svinicki. I think the -- and thank you all for being here today and for what you do.

I want to kind of dive into the language on some of these slides because I think it's very interesting. And I want to probe just a couple of things here.

And I guess I'll start off with Ms. Martin. At the top of page 65, the subcommittee recommends that extravasations should be considered a type of passive patient intervention. Is that always a type of passive patient intervention, so it's never a misadministration, for example?

MS. MARTIN: As far as I'm aware and as far as this committee is aware, I would certainly say that is it. I don't think anyone in the medical field is going to purposely misadminister or cause an extravasation.

As far as I'm aware, that is a patient intervention from a problem with the patient's physiological status.

COMMISSIONER HANSON: So there is never a medical error, of course, not --

MS. MARTIN: I am not aware of a medical error when it comes to extravasations. I'm sure -- like I said, I don't know of anyone that would certainly do it on purpose.

COMMISSIONER HANSON: Of course.

MS. MARTIN: I'm sure they -- all extravasations, I mean, you can -- you know, when you're trying to make those injections would depend on whether you say, yes, there is some people that are just hard to hit the vein correctly would be how you would define that. But I don't think it is a purposely caused medical error.

COMMISSIONER HANSON: Right, no, of course not purposely caused or intentional, right. I'm not trying to --

MS. MARTIN: Correct.

COMMISSIONER HANSON: -- ascribe intention. And yet, errors happen. Sometimes you don't sink the putt or hit the ball or --

MS. MARTIN: Correct.

COMMISSIONER HANSON: -- whatever, score the touchdown. I don't know. Sometimes you fumble or there's an interception. It happens.

Okay. Well, I guess I have kind of a similar question on page 75.

MS. MARTIN: Well, wait --

COMMISSIONER HANSON: Go ahead.

MS. MARTIN: -- I think some -- go ahead --

MR. SHEETZ: This is Mike Sheetz. May I comment on that --

MS. MARTIN: Yeah.

MR. SHEETZ: -- Commissioner Hanson? I think the performance of injection is a combination of technical skill and navigating the patient's anatomy.

Prior to going into radiation and taking health physics, I was a

practicing nuclear medicine technologist a number of years ago. I performed thousands of intravenous injections. Some of those resulted in extravasation. Sometimes I realized it. Other times I didn't, and it appeared on the image.

It's very difficult to tease out whether it was an error on the part of the person performing the injection or the patient's anatomy such that it was very challenging or difficult to get a needle into the vein or the vein tore or in removing the needle there was some leakage out.

So there are so many different variables and factors. I think it would be very difficult or, again, as I keep going back to, this is a practice of medicine issue. And it really should not rise to a medical event reporting unless it results in permanent functional damage. Thank you.

COMMISSIONER HANSON: Thank you, Mr. Sheetz. I think that's a really interesting point. And I want to just kind of drill down on that even just a little further, because I think we have kind of similar language on page 75 where exceeding the medical event dose threshold doesn't indicate error or harm.

Does it not -- again, is that a never or is that a never statement or a not necessarily statement, so exceeding the ME dose threshold doesn't necessarily indicate error or harm, or does it not ever exceed error or harm?

MS. MARTIN: Well, I'll take a first answer at this. I think it's a, it is not a never, because, like we said, if you, particularly with some of these more potent therapeutic agents in a very small area, you can get the dose up to a level that you could potentially cause at least ulceration or something.

But most of the time, that is a not necessarily comment. In

other words, exceeding the 50 rem does not necessarily mean permanent functional damage.

MR. SHEETZ: This is Mike.

COMMISSIONER HANSON: Yeah, thank you. Go ahead --

MR. SHEETZ: May I comment also?

COMMISSIONER HANSON: Yeah.

MS. MARTIN: Yeah.

MR. SHEETZ: Exceeding 50 rem or at 50 rem, it will not cause any tissue damage no matter where it is.

MS. MARTIN: Yeah.

MR. SHEETZ: So you can exceed the dose threshold for reporting the medical event, and there will be no harm to the patient.

There will be harm if the dose gets great enough. And I would say that would almost be exclusive to the therapeutic radiopharmaceuticals and would be very, very rare for a diagnostic radiopharmaceutical to reach the level of patient harm or tissue damage. Thank you.

COMMISSIONER HANSON: Thank you. Thank you both very much for that.

I think I want to follow up on that, because I think some of the language here that we're kind of talking about is the language of medical liability. And I think that's kind of bleeding into regulatory and practice of medicine type of language.

And I think that's, at least for me, part of what's confusing and difficult to tease out in this issue. So, whenever we talk about errors, there's

often talk about, well, who made the error and whose fault is it and was there any damage and so forth.

And I'm concerned that, for instance, by not, say, reporting -- you know, there's kind of a categorical statement on page 77 about, you know, that medical events resulting from patient intervention, which I think is kind of the bucket where all of these things are falling into, would not improve the practice of medicine.

And I'm finding that, and would not, it would potentially infringe and wouldn't actually help prevent the occurrence of these events in the future. That seems confusing to me.

If we had information about how these events are occurring, whether on the patient side or the administration side, whether they rise specifically to the level of medical events or not, how could that not improve the practice of medicine and not prevent them from occurring in the future, at least in some way, even on the margins?

MR. SHEETZ: If I could respond to that, again, the causes for extravasation are, you know, varied, and again, depending on technical ability and patient anatomy.

I'm not sure you would get a medical event report, the actual root cause analysis, of what the reason was and would just get it extravasated and it exceeded the dose threshold. So I don't see that information coming back to the licensees and providing any benefit.

MS. MARTIN: I would support that answer, too. You can say you had an extravasation. But that's not necessarily going to cause. There's not a transference from one patient to the other. So, in other words,

just because it happened on patient 1, you're really not going to prevent it from happening on patient 2, if you happen to have two patients with problem veins.

COMMISSIONER HANSON: Okay. Well, let me kind of take a different angle on that slightly.

In the 2019 report on the subcommittee on extravasations, it said the prevention of extravasation is a medical training issue. So, if it's a medical training issue, why do we call it a passive patient intervention?

MS. MARTIN: Well, Mike is actually the one that's been through the training. But I've been on the teaching end of it but not doing the actual needle training.

My understanding is whether you're a nursing student or whether you're a nuclear medicine technologist, they all go through the basic training on how to do injections. Mike probably has more information than I do on that.

COMMISSIONER HANSON: Presumably even on people with bad veins, right? I mean --

MS. MARTIN: Correct.

COMMISSIONER HANSON: -- there are probably different approaches and techniques and so forth, right?

MS. MARTIN: Yes. I happen to have a nurse, a niece that's an RN. And, I mean, we've gotten into this discussion fairly often. And that was when I learned a little bit about what all training they went through.

And I know the nuclear medicine technologists in the programs I've been involved with do basically the same training. In fact, they're trained on patients with difficult veins because they know that many of their

patients are going to have the difficult veins.

Mike, do you have any, as a nuclear medicine tech, do you have anything to add to that?

MR. SHEETZ: Not really. Training components, certainly you have to learn how to perform injections.

MS. MARTIN: Yeah.

MR. SHEETZ: And then the skill level increases with the more you perform and the more different types of challenging veins that you encounter.

So, again, that's why we caution this is not something to try to regulate, you know. And now you're regulating the person's skill level.

So certainly there should be the basic instruction and training on how to perform injections. All nuclear medicine technologists receive that, physicians receive that. And then you acquire more skill the more administrations you do.

COMMISSIONER HANSON: Okay. Thank you. Thank you both very much.

CHAIRMAN SVINICKI: Thank you, Commissioner Hanson.

Well, my colleagues' questions have been very illuminating. And I'm struck by that old saying of everything's been said but not everybody's said it.

I could return to some of my questions. But maybe I'll just kind of elevate this in the sense that I'm not a medical practitioner. I'm not a medical expert.

And yet, things that we've been talking about today that fall

within the domain of, and, again, I think Commissioner Caputo quoted it directly, but, you know, radiation safety around occupational things for medical workers and looking at that, of course, we do get into the area of medical event reporting.

So, ironically I'm sure to many, our medical event reporting is not necessarily linked to patient harm or overall negative patient outcomes. But, again, that was explained.

It might have been Commissioner Caputo or others who talked about the fact that what we're trying to do is bring to light things that are systematically, programmatically maybe deficient. And, therefore, our regulations are meant to bring those forward or identify if it's occurring either with individual practitioners or maybe the program of a large medical facility.

And then our regulations would, once bringing those out into the daylight, hopefully get the examination so that corrective actions or training or things could be taken.

But a lot of the focus at least in this particular meeting with the ACMUI has been on some of these things that really get very, very close to patient care.

If I begin with Dr. Jadvar's presentation, which was the final presentation, and we looked a bit over the horizon, I mentioned that it seemed that many of these trials were having very promising results.

Frankly, as he was delivering the presentation, I was looking at some of the scans and the patient response, and I thought -- I don't know. The word that comes to mind is borderline miraculous in some of these cases. And I understand that there are very rigorous trials that need to be completed.

But the public policy objective, or one of many, that's broader than the NRC would be to make these promising things, if they prove out affordable, available, you know, kind of in settings where the right amount of medical care and radiation safety was put around them, but not excessive elements that made them less available, less affordable, and, therefore, their promising results, you know, are not available to as many patients who could benefit.

So I think what we are trying to do with trying training and experience, you know, is look at kind of the right set and have a routine or, you know, a periodic reevaluation of that.

And when I think about all the things that Dr. Jadvar presented, if those things proved out, it looks like to me as a person, not an expert in the area, that there could be growing applications in both the diagnostic and therapeutic area, which in a perfect world would be able to be administered not just in major medical, you know, centers in the United States but maybe in communities at least of medium size.

And we've talked a lot about this issue of shortages of authorized users. And, you know, if I reflect on all my years on the Commission I think about how -- this may sound a little bit unfair, but we keep coming back to, it's like, well, we don't have data of where it's not available and our authorized users. It's like this proving of a negative.

And if we, again, return to that public health objective of having the right set of regulations that allow these things that are promising or prove out to be administered and available to the broadest possible set of patients with the least, you know, amount -- and I don't mean that least like

we're cutting corners. I just mean the appropriate amount of training and experience or requirement.

And I did take note, in one of the reports, there was a discussion that like even unit dosing is not really a reason. You still need the full complement of medical and radiation safety training around everything.

You know, as we look at this pandemic and we have promising, we hope, vaccines on the horizon, one of the things that the logistics of deployment is about is, you know, how could we get the largest number of authorized pharmacists and people that can administer the vaccine. Once it's ready it can be distributed amongst the population as quickly as possible. So there's some parallels there.

And I was going to ask about the minority opinion on training and experience. But I think the question was already posed.

But there's a kind of intuitive allure a little bit of moving away from tracking the specific physician authorizations. If this is such an area of promise for medicine, then does that just become such a cumbersome regulatory orientation that you would somehow want to?

So I don't know enough to know. And the committee didn't maybe spend a lot of time on the minority opinion, other than to note that it was a minority, so it obviously was not embraced by the subcommittee as a whole.

But that being said, it also I think came a little late and was not central to what the subcommittee was looking at in the main. So maybe they didn't spend as much time on it.

I do, as a member of the Commission, support continuing to look at the 700 hours, to continue looking at training and experience.

Maybe I'll ask this question. And it's borderline philosophical. What are the things, given that if this is a promising area of research and development in terms of nuclear medicine both for diagnostic and therapeutics, what would trigger really looking at different approaches to training and experience or how the NRC touches on this area of nuclear and radiation safety?

I just -- it seems that we keep returning to it. And maybe in the absence of either being compelled to make a change, because although there are new modalities, they are, you know, they're growing at a pace where we can keep feeding the pipeline of the various physician specialties, and, but if there were truly kind of game changer things out there that you would want to say we need to make a step change in the availability of getting something out there.

We're going to keep returning to it every, you know, five or ten years and just saying this is generally the way we should approach this. NRC's trying to look at innovation in all areas of its regulatory framework.

And so, if it doesn't really need fundamental changing today, what would be signs and indicators that we should begin to look at that? I don't know if anyone would like to offer some commentary along those lines.

DR. SCHLEIPMAN: This is Robert Schleipman. Thank you.

I think that the current recognized boards, such as the nuclear medicine community, the radiation oncology community, are very much champions of the theranostics. And they built this and are building this into their training programs. It's part of those 700 hours. But it's with focus on these newer technologies so that these are being addressed in the training and

competency of trainees.

Dr. Jadvar may have additions to that.

DR. JADVAR: I second that. Yeah, that's correct. Right now, for example, with the recent approval of Lutathera, which is basically the, after radioiodine is the first theranostic after a long time.

This is completely incorporated into our training. There are questions being presented in the boards' examinations by, in the ABNM, ABR, and also, I believe also for radiation oncologists.

So it's being incorporated as they are developed and available in the clinic. And they are also being taught about some of the future potential theranostics that I already mentioned in my presentation.

So they are definitely on top of this. And they recognize that they're championing this field and make sure that the training is appropriate for people who are going to be practicing this in the future.

And I think Melissa Martin had also her hand up. Melissa?

CHAIRMAN SVINICKI: Oh, I think you might be muted.

MS. MARTIN: Thank you very much. I will learn how to operate the mute button.

As one of the people that's been, as one of the physicists on the ABR's question-writing committee for several years, I would just reiterate that the current trainees that pass the American Board of Radiology exams have this inherent training spread out over their entire training period.

I think it is very different when you are talking about trying to take a particular drug and say, oh, we just want limited training.

I've had experience with non-radiologists, non-nuclear

medicine physicians administering some of these drugs, particularly iodine-131. For a while, there were a fair number of endocrinologists that gave these drugs without involving the radiation oncologists.

It was not uncommon to spend an inordinate amount of time as the radiation physicist and radiation safety officer answering the patients' questions trying to clean up some of the things that happened in the room.

That basic radiation safety training in radiation physics is just not part of their curriculum. And I think I would just really support the idea that that basic training has to stay in the training for whoever is an authorized user.

CHAIRMAN SVINICKI: Well, and I appreciate that, Ms. Martin. And maybe that's really a central point to return to. And please don't misunderstand me. I'm not looking to cut it close.

I mean, patient care is, it isn't just, yeah, someone with an injectable going in and not understanding what if the patient begins to have an adverse reaction.

Some of the reason that I take comfort in the views you all have expressed on extravasations is that these are patients that are receiving medical care. They wouldn't be having these isotopes and things administered to them.

And, therefore, if there can be a visual cue and then there's follow-up care and everything else, it does kind of seem to draw one to a conclusion on extravasations that you could have tons of reporting around it. It is a little bit of an elusive physiology of the patient question. It is skill of the craft of the person doing the injection.

But at the end of the day, what we care most about I think is

patient harm. So what we want to do is be able to follow up and know if this became something that was causing some concern for the patient.

And in most cases, it sounds like it would not be, because there's a lot of physiological processes going on that lead to the ultimate biodistribution of the isotope after the event occurs.

But I think we all want an extremely strong safety net and safety culture around the practice of nuclear medicine.

I think it is important that as a Commission and as a nuclear regulator we continue to probe the level of requirements that we are putting around these things and continue to look at them critically, not just is what we're doing working, but are there recommended changes that need to be made.

So it is -- and I'll kind of end with where I started. To me and I think to members of this Commission, to hear from practitioners and specialists on this committee is very, very important. We can kind of look at nuclear phenomenology, but this is people at the end of the day. And it's health care and medical care.

So we do give a lot of substantive weight to the dialogue that we have with you as a result of this meeting and also the written reports that you provide that I know all members of the Commission review prior to this meeting and that informed our questions here today.

So I thank you all again. And seeing that no one on the Commission is trying to give me a sign to be recognized, I will thank you all again for the work you do. And with that, we are adjourned.

(Whereupon, the above-entitled matter went off the record at 12:07 p.m.)