UNITED STATES

NUCLEAR REGULATORY COMMISSION

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MEETING WITH THE ADVISORY COMMITTEE ON THE MEDICAL USES

OF ISOTOPES

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THURSDAY,

APRIL 4, 2019

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ROCKVILLE, MARYLAND

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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

STEPHEN G. BURNS, Commissioner

ANNIE CAPUTO, Commissioner

DAVID A. WRIGHT, Commissioner

ALSO PRESENT:

ANNETTE VIETTI-COOK, Secretary of the Commission

MARIAN ZOBLER, General Counsel

ACMUI MEMBERS PRESENT:

CHRISTOPHER J. PALESTRO, M.D., Chairman

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

VASKEN DILSIZIAN, M.D., Member

RONALD D. ENNIS, M.D., Member

RICHARD L. GREEN, Member

MELISSA MARTIN, Member

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

ZOUBIR OUHIB, Member

ARTHUR SCHLEIPMAN, Ph.D., Member

MICHAEL SHEETZ, Member

MEGAN L. SHOBER, Member

LAURA M. WEIL, Member

ACMUI NON-VOTING MEMBER PRESENT:

HARVEY B. WOLKOV, M.D.

P R O C E E D I N G S

9:59 a.m.

CHAIRMAN SVINICKI: Good morning, everyone, I call the Commission's meeting to order. This morning we have one of our periodic meetings with Members of the Advisory Committee on the Medical Uses of Isotopes.

We'll hear about a number of topics this morning.

Before we begin, however, I would note that two Members of the Committee, and especially the two sitting at the table before us today, including the Chairman of the Committee, this will, unless something unexpected happens, be their last appearance before the Commission in a public engagement such as this meeting.

I think both have a few homework assignments and things and continued engagements with the agency but I wanted to pause for a moment just to particularly thank Dr. Christopher Palestro and Ms. Laura Weil for their contributions to the Committee. Both have been on the Committee since 2011 I believe, and so for eight years. Since that overlaps with my time here I have been the beneficiary of your insights and perspectives on important and, without exception, complicated issues in the medical area that come before our Commission.

And I want to express on behalf of the Commission and myself that these perspectives and insights, they provide a unique role for us because we are not principally a medically-oriented regulatory agency.

And so I find and have found such special and particular value in the service of the Members of this particular Advisory Committee, and to you both, again, my personal gratitude and the Commission's gratitude for

your service, but my personal gratitude. I know that your insights and perspectives have benefitted me as I have considered matters over the course of your long service on the Committee. So, we certainly wish you well and thank you both.

And I didn't know if any other Member of the Committee or the Commission wanted to just join in? Everyone joins in, okay, there we go.

All right, well, again, thank you and it isn't like you're disappearing today but this is a chance for me to publicly recognize your contribution, so thank you very much.

COMMISSIONER BARAN: Chairman, since we're doing public recognitions, we wanted to do this last Thursday but you were not here, you were not able to attend. Last Thursday, I don't know how many of you know this, was a big day.

11 years ago to that day on March 28, 2008 the Chairman was sworn in as a Commissioner. Over the course of its 44-year history, 37 individuals have served on the Nuclear Regulatory Commission and you are the first to serve 11 years.

In fact, you broke the NRC record for longest-serving Commissioner on December 8, 2018. You are also the only NRC Commissioner to have been nominated to serve on the Commission by three different presidents.

During your -- this is going to sound like a lot of days -- 4,035 days on the Commission, you served alongside a total of 11 Commissioners.

That's almost a third of all the individuals who have ever served on the Commission, and before being designated as NRC Chairman yourself, you served with four prior Chairmen.

Of course you're not going anywhere anytime soon, so every day you serve on the Commission you will be setting a new record. But last week was special because it was your anniversary.

To mark the occasion, your current colleagues want to present you with a little something, and it has magically appeared.

This engraved vase reads: Christine L. Svinicki in recognition of your performance and extraordinary leadership as the longest-serving Commissioner in the history of the NRC. Congratulations.

(Applause.)

CHAIRMAN SVINICKI: Okay, yes, that's true. If we put it on the table it would be an irregularity in the webcast so we wouldn't want that. Thank you very much and I think United Airlines owes you all an apology for -- I had some difficulties in my return which is why I was not here on the anniversary date. But that's certainly very touching, thank you all.

Longevity is always a thing to feel good about I guess but I think like all of you and the Members and Chairmen that I've served with, what keeps you going is colleagues, is the wonderful staff here at the NRC, and coming here every day and seeing how as a Commission and as individual contributors and as Members of team NRC we can make a difference here.

So, the people are what make the years go by so fast and somewhat unnoticeably, and yes, 4000-something sounds like a whole lot. I will take that on board but thank you very much for that really gracious recognition. It's a please to serve with all of you.

And now that all these salutations and commendations have been dispositioned, let us begin with, again, the very important topics that will be presented today by Members of the Advisory Committee on the Medical

Uses of Isotopes.

And I think if you would prefer, Chairman Palestro, I will probably turn over to you and then allow you to maybe recognize the Members of the Committee and the topics in the order in which you've agreed amongst yourselves to present. So, the floor is yours.

DR. PALESTRO: Thank you, may I have the slides, please?

Madam Chair, Members of the Commission, I=d like to express gratitude on behalf of the ACMUI for once again having an opportunity to appear before you and share with you some of our activities over the past year.

And for that we are most grateful.

I'm going to begin with an overview of the ACMUI. Next slide, please. And I'm going to review for you our role, our membership, some of the topics that we have covered and are covering, as well as our future directions.

Next slide, please.

The ACMUI's role is to provide advice on policy and technical issues that arise in regulating the medical use of radioactive material for diagnosis and therapy, to comment on changes to NRC regulations and guidance, to evaluate certain non-routine uses of radioactive material, to provide technical assistance when and if requested, and to bring key issues to the attention of the Commission for appropriate action.

Next slide, please. There are 13 Members on the ACMUI with very diverse backgrounds and that is designed to encompass the diversity of topics and issues with which we are faced. All of these individuals have expertise in their various areas. They include a healthcare administrator, Dr. Arthur Schleipman, a nuclear medicine physician, myself, two radiation

oncologists, Dr. Ronald Ennis and Dr. Harvey Wolkov.

Dr. Wolkov is undergoing clearance currently. A nuclear cardiologist, Dr. Vasken Dilsizian, a diagnostic radiologist, Dr. Darlene Metter.

Next slide.

Two medical physicists, one nuclear medicine, Ms. Melissa Martin, one radiation therapy, Mr. Zoubir Ouhub, a nuclear pharmacist, Mr. Richard Green, a radiation safety officer, Mr. Michael Sheetz, patient rights advocate, Ms. Laura Weil, an FDA representative, Dr. Michael O'Hara, and Agreement States Representative, Ms. Megan Shober.

Next slide, please. Some of the topics that we have addressed and are addressing at the moment include an analysis of medical events, and you're going to hear more about this from Dr. Ennis a bit later.

I think this is a significant addition to our program because while we reviewed medical events on a yearly basis in the past, this is the first time that we're starting to take both a look back and forward at these events, looking for trends in their causes with the ultimate goal of being able to reduce the likelihood of these events occurring in the future.

So you're going to see some of the initial data today and I think it holds great promise for the future.

Another topic was the American Brachytherapy Society's Medical Event Case Study Program, a program designed to help individuals reduce the likelihood of medical events in their practice. A review of non-medical events, an ongoing review of Training and Experience for All Modalities, which you're going to hear from Dr. Metter in a little while, a draft revised of the Leksell Gamma Knife Perfexion and Icon, compounding of sterile and non-sterile radiopharmaceuticals.

Next slide, please. Nursing mother's guidelines, which Dr. Metter also will go over with us, a review and an update of the ACMUI bylaws, the appropriateness of medical event reporting, Yttrium-90 microspheres brachytherapy licensing, and ACMUI external communications.

The ACMUI External Communications Program was started a few years ago by my predecessor, Chair of the ACMUI, Dr. Philip Alderson. And the goal of this venture, if you will, was to enhance communications between the ACMUI and professional organizations.

And I'm pleased to report to you that in June, for the third consecutive year, the ACMUI will have a full session at the annual meeting of the Society of Nuclear Medicine and Molecular Imaging.

In July, the ACMUI will also have a session, Mr. Sheetz and Ms. Holiday will be attending at the meeting of the Health Physics Society in Orlando, Florida.

Next slide, please.

While it may seem that what I've presented, or while it may seem from what I have presented that it's the ACMUI doing all of the presentations, in point of fact there's always an ongoing dialog and an intimate close-working relationship between the Members of the Committee and the staff.

And I think that the staff presentations also should be highlighted, and they include the Training and Experience Stakeholder Outreach Plan, a review of the ACMUI's reporting structure, a summary of the medical-related events for the past year, a summary of changes to 10 CFR Part 35, the Yttrium-90 microspheres brachytherpay licensing guidance, the medical team highlights, and how the ACMUI and its Subcommittees work together with

the NRC staff and management under the Federal Advisory Committee Act.

Next slide, please. In the future, the ACMUI will continue to provide advice and technical assistance, to comment on NRC regulations and guidance, to evaluate the uses of radioactive material, and to bring key issues to the attention of the Commission.

Next slide. The rest of today's agenda, Dr. Darlene Metter, the ACMUI Vice Chair and Diagnostic Radiology Representative, will offer comments on the guidelines to nursing mothers for exposure from the Medical Administration of Radioactive Materials.

She will also offer comments on the Training and Experience Requirements for All Modalities. Dr. Ronald Ennis, the ACMUI Radiation Oncologist of Brachytherapy will provide a review and analysis of the reported medical events for fiscal years 2014 to 2017.

Next slide.

And finally, Ms. Laura Weil, the ACMUI's Patients' Rights Advocate will present her perspectives on the Nursing Mothers' Guidelines, the Training and Experience Requirements for All Modalities, and medical event reporting.

Next slide, please. And now I will turn it over to Dr. Metter. Thank you.

DR. METTER: Thank you, Dr. Palestro, and thank you for inviting us here to speak with you today. May I have my slides?

So today I'm going to be talking about the guidelines to nursing mothers in regard to radiation exposure from the Medical Administration of Radioactive Materials.

Next slide, please. Our Subcommittee Members are Dr.

Vasken Dilsizian, myself, Dr. Christopher Palestro, and Dr. Pat Zanzonico. And our Resource Staff is Maryann Ayoade.

Next slide. So the charge of this Committee was to review the radiation exposure from diagnostic and therapeutic radiopharmaceuticals, including brachytherapy, to the nursing mother and child.

Next slide. Now, radiation therapy, radionuclide therapy, is targeted to destroy disease tissue and, therefore, it's very important that we be very careful in what we do.

Breastfeeding is not regulated, however, at times it is necessary to administer radiopharmaceuticals to the nursing mother. And many times, many of these agents appear in breast milk. So, with that, in regards to -- may I have my slides, please? -- 10 CFR 35.75 and in regards to the patient, and in this case the nursing mother, patient can be released if the total effective dose equivalent to the nursing child is less than 5 millisieverts.

If the exposure could exceed 1 millisievert to the nursing child, written instructions of adverse consequences must be given if nursing is not stopped and guidance to the mother on the discontinuation of breastfeeding.

Next slide. Now, most mothers who are administered radiopharmaceuticals require temporary cessation of breastfeeding. However, a few nursing mothers administered radiopharmaceuticals may require a complete cessation of breastfeeding.

Next slide. A major exception, however, is I-131 sodium iodide mainly this is to decrease the breast dose to the mother. And what happens is when the mother who is nursing receives 1-131, it gives a significant dose to the maternal breast as opposed to the non-lactating breast.

For example, if you look here, if a nursing mother is administered 150 millicuries of I-131, that delivers 200 rads, a huge amount, to the maternal lactating breast. So, to decrease the breast dose lactation must cease and that takes about six weeks.

Therefore, breastfeeding must stop six weeks prior to radiopharmaceutical administration of I-131 to cease lactation and then also permanently for that child. In the future, however, the mother may breastfeed for her future children.

Next slide.

Now, when you actually look at the radio exposure during nursing to the mother and to the child, to the mother it's internal administration, it's an internal source as far as regarding the administration of the radiopharmaceutical.

To the child, the child actually has two sources, an external source and an internal source.

Next slide, please. The external source is the mother. She's a significant radiation source especially during routine childcare which entails close prolonged contact with the child.

And as you know, our ALARA principle, which is our basis for radiation protection, as low as reasonably achievable, the time spent in childcare is prolonged which increases the dose to the child.

And as our ALARA principle, we like to decrease that time period. And the distance is very close proximity in childcare so that clearly increases the dose to the child.

And as you know, radiation, the further away you get, the less radiation gets. So really, childcare has a significant radiation exposure to the

nursing child. Next slide. So, the internal source is going to be to the child the ingested radioactive milk. Well, you say how much radiation does that make? Well, it depends on the radiopharmaceuticals. Generally, less than ten percent of pharmaceuticals administered to a nursing mother enters the breastmilk and on average it's about 0.3 to 5 percent. The major exception is I-131 sodium iodide and as I mentioned, causes a significant increase in dose to the lactating breast.

And in some cases this is a very high accumulation, 25 percent of the administered dose. So it's really best to cease breastfeeding six weeks before administration of I-131, and again, permanently for that child, however, the mother may nurse other children in the future.

Next slide. So the Subcommittee made this table in regards to individuals who decide to administer radiopharmaceuticals to the nursing mother because it's necessary.

And this gives a table about nursing interruption and the radiopharmaceutical to help our healthcare providers in giving the best care in regards to safety for their patients.

Nursing must stop for I-131 sodium iodide and, again, six weeks prior to the therapy. Nursing must stop for I-124 sodium iodide, all alpha agents, and for 177-lutetium.

No interruption is needed for the very short-lived radiopharmaceuticals of oxygen-15, rubidium-82, and germanium-68, one hour for carbon-11 and nitrogen-13, and four hours for fluorine-18.

Next slide, please. 24 hours for 99-technetium agents, 3 days for 1-123 sodium iodide, 4 days for 201 thalium, 6 days for indium-111 white cells and octreotide, and 28 days or about a month for gallium-67 and

zirconium-89.

Next slide. For Y-90 microspheres, no interruption is needed and for breast and sentinel lymph node sources once they're removed, no interruption, as long as the sources are not in the nursing mother.

Next slide. So it's also very important that the Nuclear Medicine Department has signage and this is to inform the nursing mothers or mothers planning to nurse in the near future who are scheduled for a nuclear medicine procedure.

And this is important that they are informed that certain radiopharmaceuticals may require certain radiation safety precautions. And such patients are advised to notify the nuclear medicine staff and physician prior to the nuclear medicine procedure.

Next slide. On February 1, 2018 the ACMUI had a public teleconference call. During this call, the ACMUI unanimously approved the submitted report with some caveats and these are just regarding calculations and certain modifications on the tables. During our fall meeting on September 20, 2018 the ACMUI unanimously approved the revised report with additional language regarding FDA-approved radiopharmaceuticals and the need to evaluate radiopharmaceuticals not encompassed in the report.

Next slide. And these are my acronyms. The next topic that I'll be commenting on is the Training and Experience Requirements for All Modalities, 35.300 Uses.

Next slide. My Subcommittee Members are Dr. Ronald Ennis, myself, Dr. Robert Schleipman, Mr. Michael Sheetz, Ms. Megan Shober, and Ms. Laura Weil and are NRC staff Resource was Maryann Ayoade.

Next slide. So in March 2018, the Training and Experience

Subcommittee came with the following two recommendations. The first was at that time there was no objective data for current AU shortage.

The second recommendation, however, was to reconsider an alternate AU pathway under 10 CFR 35.390 because the Committee wanted to proactive rather than reactive with a recent turn of events which they observed during that time.

And this was number one, in January of 2018 the FDA approved 177-lutetium dotatate, which has the potential for greater clinical use and more therapies.

And second, there was a decrease in the number of first-time candidates sitting for the American Board of Nuclear Medicine certification exam. So again, being proactive, they were concerned that maybe there may be a potential shortage of AUs in the future.

Next slide. So let's look at that. Next slide. The current pathways to become an authorized user, there are two as far as regarding 10 CFR 35.390. Pathway 1 is considered the Board certification pathway and this is where the NRC deems status Boards and these are the American Boards of Nuclear Medicine, Radiology, and Osteopathic Radiology.

When you pass these certification exams, you then are qualified to become an authorized user under 10 CFR 35.390. And currently, there are two programs that fall under this category.

These are the nuclear medicine and radiation oncology programs. So, again, graduates who complete these programs and pass the certification Board of the respective Boards as listed become authorized users under 35.390.

Next slide. The second pathway is called the alternate

pathway and this is where an individual in training completes 700 hours of training and experience including classroom and laboratory hours and basic radionuclide handling techniques, the medical uses of unsealed byproduct material requesting a directive.

And under this category, there are two current programs: the diagnostic radiology, the redesigned pathway. And this was approved by the American Board of Radiology in 2010 and it entails 16 months of nuclear medicine during a 48-month diagnostic radiology residency.

The second is the Nuclear Radiology Fellowship and it's a one-year program that is completed after four years of a radiology residency.

Next slide. So when you actually look at the number of potential trainees in the pathway to have 35.390 and if you look at pathways 1 and 2, in training there are four, actually, residency programs that incorporate these individuals.

In nuclear medicine, nuclear radiology, the redesign pathway and radiation oncology the potential number of individuals who will be able to become authorized users for 35.390 is 921.

If you extrapolate that, just an estimate as far as number of graduates per year, the total is almost 270. So if you go further out, in four years you have over 1000 new individuals who will be able to perform therapies under 35.390.

Next slide. So, is there an AU shortage? Let's look at the numbers. In the current academic year of 2018, the pipeline for 35.390 is over 900 graduates. For 2019, about 270.

And in 2018, the American Board of Nuclear Medicine looked at the diplomats in the number and there are 3591, almost 3600, practicing

authorized users. So, in 2019 when we actually looked at the data, there was no objective evidence for an authorized user shortage.

Next slide, limited scope pathway. As I mentioned, radionuclide therapy's goal is to destroy disease tissue. Now, with that, radionuclide therapy then poses the highest risk and highest impact of any of our nuclear medicine procedures and, therefore, it has to be performed properly.

If it's improperly performed, you can have severe unintentional damage or destruction of organs or tissues. Therefore, to protect the public and safety, anyone who does radionuclide therapy must have a basic minimal level of competency to protect the patient and be safe.

In addition, not only the acknowledged topic and the Training and Experience, the limited scope and a full authorized user must have an equivalent level of competency for that radionuclide therapy.

Next slide. So when we actually sat down and looked at the feasibility of a limited scope authorized user, we started with what do you need to know to be safe?

What's the minimum level of knowledge and training you need to be safe to deliver radionuclide therapy? And pretty much it's a total novice topic in 35.390.

And then we looked at the individual radiopharmaceuticals for therapy and each individual radiopharmaceutical has their own conflict radiation safety issues.

And if you actually again look at it, it's so complex there's multiple overlaps in topics that you have to learn. So any category would clearly include the prior radiopharmaceutical knowledge base you need and be

a carbon copy of all the other pharmaceuticals.

So with that, rather than just repeat for this therapy one, you need this knowledge topic or experience this second radionuclide, which is, oh, by the way, the same thing as the previous one.

The Subcommittee concluded that it was not feasible to recommend a limited scope authorized user pathway.

Next slide. So our final recommendations. The Committee strongly supports the current AU pathways for 35.390 which protects the public's health and safety. There is no objective data to support an authorized user shortage.

Next slide. The Committee does not recommend a limited scope AU pathway for the reasons I discussed for unsealed byproduct material, for which a written directive is required.

Next slide.

The Committee agrees that if the NRC pursues a limited scope AU pathway despite the ACMUI recommendations, the authorized user candidate must attest to the acquisition of the basic knowledge topics of 35.390 and the skills to successfully complete a formal competency assessment with continued formal periodic competency reassessment.

And this would be to maintain their limited scope AU status.

Next slide. On February 26, the ACMUI approved the report and its recommendation with one revised to add the language below.

And this says the Subcommittee will work with the NRC if the NRC decides to pursue a limited scope pathway, and again, against our recommendation. But we're willing to work with the NRC staff to develop an AU curriculum of knowledge topics. Next slide. And these are acronyms. And now

I turn it over to Dr. Ennis.

DR. ENNIS: Thank you, Dr. Metter, and good morning to the Commission. Thank you so much for your attention and the opportunity to speak with you today. Slides, please?

My topic is going to be a review of medical events to share with you some insights that the ACMUI has gleaned from review of events over the years 2014 to 2017.

As Chairman Palestro alluded to before, the ACMUI yearly reviews all the medical events as does NRC staff. But this year we decided to broaden the look and look at a group of years to start to looking for something more meaningful.

Thankfully, there are relatively few medical events per year. As you well know, there are approximately 150,000 uses of radiopharmaceuticals and medical isotopes per year and a very small proportion of medical events.

Nevertheless, we are committed to driving that as low as possible but the only way to do that meaningfully is to look at a larger group of events. So that's what I'm going to share with you.

Our Subcommittee was myself, Mr. Richard Green, Dr. Metter, Dr. O'Hara, Dr. Suh, who just rotated off of ACMUI, and Mr. Sheetz, and we were supported by Sophie Holiday.

Next slide, thank you.

So, the approach here was not to look anecdotally at single events and understand exactly what happened with each one, but to look for more common themes that might be within sections, within types of applications or across applications as a way to then help spread that knowledge, share that

knowledge, and decrease the number of medical events. So we reviewed four years' worth of reports that we had accrued over the last four years in the presentations we had done before for this purpose.

Next slide. And we ended up determining that we could articulate two themes that stood out, and I'll show you the data in the coming slides.

But the themes are, number one, performance of a timeout prior to an administration of radioactive byproduct material, as is done now very commonly in the medical world and before surgeries in particular and other procedures, could have prevented a significant minority of medical events.

Number two, there appears to be an issue regarding lack of recent or frequent performance of specific administrations, and that seems to be a contributing factor in a number of cases as well.

Next slide. So now we'll look at the data within each of the various administration categories. So, for 35.200, unsealed byproduct material for imaging and localization, these are the number of events over the four-year period. And in total, 21 events over the four years.

And they were really broken up into three groups really, I categorized all of them, either the wrong drug, the wrong dosage, or the wrong patient. And many of the wrong drug and wrong dosage were overlapping events.

Next slide. In thinking about these three categories, what would help? So a timeout could certainly have an impact on wrong drug, the effective moment of the timeout. One of the things that was reviewed is, is this the drug for this patient? Similarly, the wrong patient would also be caught potentially by a timeout and that timeout, the core to a timeout, is verified by two

means, patient identification, typically name and date of birth. Wrong dosage would not necessarily be facilitated by a timeout.

So about half of the 35.200 medical events over the four-year period could have potentially been prevented by the additional of a timeout to the procedure. So, giving the administration.

Next slide. Within 35.400 manual brachytherapy events, so we had 27 events -- I'm sorry 40 events over the four-year period. a number of them are in their prostate dose.

Prostate dose, as you know, was part of the issue that led to the revised of the Part 75 rule and many of those events would not be categorized as events now. Some still would but many would not.

In terms of other sources of medical event within the manual brachytherapy category, we have applicator issues, wrong site implantation, and activity/prescription errors such as confusing air kerma and millicuries.

Next slide. So again, with this lens in terms of total medical events, affording the timeout would have had the potential to prevent about ten percent of these events, particularly the ones regarding prescription, air kerma, millicurie, for example.

And this is a matter of judgment but our expertise looking at the medical events, we felt there was a sense of a lack of experience playing a role in approximately 15 of these medical events.

Next slide. So, this pretty much summarizes what we said before. So about 25 percent of cases, a timeout or some type of enhanced training or prior to be using common procedures, these two themes explain about 25 percent or contribute about 25 percent of the medical events within this category.

Next slide. Going to 35.600, which is seal sources in afterloader uses, teletherapy units, and gamma knife, gamma stereotactic units.

So, again, over the four-year period, 37 events and they are categorized here: wrong position, wrong reference length, which is a specific thing having to do with high-dose-rate catheters, the wrong plan, the wrong dose or source strength, and some machine or software malfunctions.

Again, looking for themes through the lens that we have described.

Next slide.

Sorry, but this is just breaking it up by parts of the body so gynecologic applications are the leading category for which that's HDR application brain is typically what we were talking, about the Gamma Knife applications.

Next slide. So, again, with this lens, the timeout overall would have potentially caught about 15 percent of these events over the time period that we analyzed.

And next slide. Again, infrequent user phenomenon, if you will, again, this is hard, it's based on an assessment of the animate information and with our expertise getting a sense of whether we thought that played a role.

And our estimates were that it was a significant issue in 35.600 with approximately a third of the events appearing to have an infrequent user issue as a contributing factor.

Next slide. In terms of the 35.1000 category, the first one within that that we'll talk about is radioactive seed localization and there are

very few events in this category.

Next slide. Within the Leksell Gamma Knife Perfexion and Icon, which are licensed under 35.1000, a relatively small number of events as well, 12 events.

A large number of them were really a single issue, a patient positioning system problem. Other than that, a couple of patient setup error issues, patient movement, wrong site.

Next slide. And the last category within 35.1000 that we'll talk about is microspheres and on this slide and the next slide are the summaries for each of the two types of microspheres that are out there, the TheraSpheres and SIR-Spheres.

And from our perspective, they were very similar in terms of the kinds of events. There are more events, not necessarily staying proportional to the -- because we don't have the denominator here but just numerically there are more events of this type. In some of the other categories, a large number of them seem to have to do with the residual activity remaining within the delivery device, the tubing, the hub, et cetera.

But there are issues related to setup and wrong dose, wrong site, shunting issues, catheter placement issues. So that's it for the TheraSpheres and then the next slide will summarize for SIR-Spheres.

And again, we're not trying to compare the two or even compare these to others, just to share that they, to our view, are fairly similar in the themes and the issues that you see with slightly varying numbers but in the same ballpark.

Next slide. So, a summary of this will tell us a little bit better so about 60 percent of the medical events in this subgroup of Y-90

administration has to do with residual activity within the tubing, the hub, et cetera.

Wrong dose is about 11 percent, wrong site is about 11 percent due to catheter placement. Shunting plays a similar role and setup area is again about ten percent.

So, next slide. Okay, medical events that might have been able to be prevented within this category based on the timeout concept. So, for the seed localization, one of them may have been prevented by performing a timeout prior to implantation of the seed.

Within the Perfexion Icon category, approximately 25 percent we thought could have been prevented by a timeout. And in the microsphere space, about 12 percent.

Next slide. And then again trying to parse out whether there was a role of lack of experience or infrequent user phenomena if you will in these categories.

It seemed as though this did not play a role in radioactive seed localization. About 15 percent of Perfexion Icon and about 10 percent, 8 percent in the microspheres.

Next slide. So, if a timeout was done, what would that look like? In this extrapolating, again, from the concept that's used in surgery and kind of having in mind the problems that we saw in this review, a timeout could include the following elements.

One, the identifying of a patient by two means. Number two, confirming the procedure to be done. Number three, confirming the isotope. Number four, confirming the activity. Number five, confirming the dosage.

And other features that would be applicable to certain

applications but not others, and therefore not necessarily part of a uniform radioactive timeout, but for certain ones would be confirming the units of activity.

In particular, not just the activity but the units because we've seen that as an LDR prostate issue and atomic location for those that are actually anatomically specific, which a fair number are.

A patient's name is on the treatment plan so not just confirming who is in front of me but is the plan that I'm about to apply to that patient actually this patient?

Making sure that the plan itself has had an independent second check, that the reference length is proper, this is a very specific thing having to do with HDR but is a common theme that we see.

So that could be added to a timeout as applied to an HDR. Have we checked the length? And implant site location, which is similar to anatomic location really.

Next slide. Now, what to do about the issue of infrequent procedures or that concept?

So, again, suggesting to the medical community that for those who are in such a situation or about to do a procedure they have not done recently or are doing but not frequently, there are a number of review courses available from professional societies that they can avail themselves of.

There are a plethora of review articles in the overwhelming medical literature nowadays that are available. Obviously, reaching out to colleagues to review the procedure, doing a dry run would be an excellent recommendation that we might be able to make to the medical community with your entire team prior to doing an actual procedure.

And reviewing your equipment, your device setup and equipment again to be sure it's working properly and that you know very specifically what to do.

Next slide. So, our Subcommittee then recommended to NRC at the September 2018 meeting this report was accepted by the broader ACMUI community and we recommended that the NRC issue an information notice alerting authorized users to the themes identified herein.

The NRC staff has accepted this recommendation and execution of this is pending resource availability.

And with that I'll turn the podium over to my colleague, Ms. Weil.

MS. WEIL: Thank you, Dr. Ennis. Thank you. Over the last nearly eight years of my tenure on the ACMUI, the subject of medical event reporting has been raised repeatedly.

We've discussed the punitive nature of required reporting, the perceived unfairness of public reporting of events that cause no patient harm, and of the failure to make use of the collective event data in a way that can be proactively beneficial as an educational tool and part of safety culture.

NMED is a regulatory database and I assume it works pretty well for its stated purpose.

But aside from the purely regulatory purpose of required reporting and NMED data entry, there's at least a theoretical hope that the subsequent required investigation will foster honest self-assessment in the reporting institution and the implementation of meaningful corrective action to mitigate the likelihood of event recurrence.

That's useful for the involved institution certainly, but it

basically ends there. As a patient advocate, I feel strongly that there's a missed opportunity here.

We'd like to see that the collected data is used more broadly for all interested healthcare providers to learn from the mistakes of others and hopefully prevent similar occurrences in their own workplaces. As stated, NMED may work well from a regulatory perspective but it's willfully inadequate for the broader educational purpose. There is simply not enough detail captured in NMED or the detail is basically inaccessible for useful learning.

NRC needs to decide if it's willing and able to engage in what may be an ambitious endeavor to upgrade NMED into something proactively supportive of safety culture.

The Nursing Mother Subcommittee provided a detailed and comprehensive report on guidelines to reduce infant exposure and maternal harm. The exposure of any nursing infant to radiation from mother's treatment should be unacceptable.

If it occurs, it's solely attributable to a failure on the part of the healthcare provider to appreciate the risks of radiopharmaceutical use.

Unlike an undisclosed or as yet un detectable pregnancy, the healthcare provider is able to and has a responsibility to identify a nursing mother.

The provider has an obligation to communicate the risks of radiopharmaceuticals effectively and allow time for the nursing mother to plan for whatever pre or post treatment precautions must be made, including cessation or termination of lactation.

Providers need a comprehensive knowledge of radiation

biology and up to date awareness of the risks of new radiopharmaceuticals as they become available, and commitment to good communication and safety. All of this is dependent on comprehensive training and experience.

The last time I offered my observations about Training and Experience requirements. I was on the fence about the benefit of finding tailored T&E requirements for certain kinds of radiopharmaceuticals.

I cited concerns about healthcare providers being protective of both professional and financial turf. I posed whether that was at least partially driving physician/organization opposition to any changes in T&E requirements, which are traditionally accomplished in medical residency trainings.

And on the other side, one can argue that there are certainly financial motivations to opening up the field with limited scope license opportunities for non-residency-trained physicians.

Concerns have been expressed about a looming shortage of authorized users. These concerns still feel relevant, however, the argument that broad experience and training with the topics encompassed in the traditional training pathways serves patients better, that's a compelling argument.

Given the potential for proliferation of new radiopharmaceuticals and the complexity of most of these administrations, they're best delivered in the context of comprehensive knowledge and expertise. And since the U.S. healthcare market is market-driven, we have to assume that the market will drive more physicians into training programs to become authorized users of a proliferating market segment. Will some patients have to travel to access this expertise? Yes, they will. And will

that create insurmountable barriers for some of these patients? Yes, it will.

But it's not the role of regulation to create access. The role of regulation is to create safety. And that delicate balance point is in making sure that regulation does not create unnecessary barriers.

Healthcare providers who wish to offer radiopharmaceuticals to their patients need to be a competent to do so.

The competence is dependent on a wide range of knowledge and experience, and in addition, regulation regarding the measurement of such competence and the maintenance of competence needs to be manageable and enforceable.

Creating separate T&E thresholds for each existing and in-the-pipeline radiopharmaceutical could cause a regulatory nightmare that might well compromise patient safety and public safety.

I=d like to offer some final thoughts. This is my last ACMUI meeting and Commission briefing and I would love to express my gratitude for your interest over the past years in hearing an advocacy perspective at these briefings.

It's worth stating that I consider all my colleagues on the ACMUI to be patient advocates, and very rarely have I felt that the consideration of patients' rights or the ethical perspectives of advocacy have been at odds with the opinions and positions of the Committee as a whole.

It's been an honor to serve on the ACMUI and I thank you for the opportunity to talk to you.

CHAIRMAN SVINICKI: Well, thank you again to each presenter for the presentations and to each of the Subcommittees for their work in the Committee as a whole.

It's the practice of our Commission to rotate the order of questioning and today we begin with Commissioner Burns.

COMMISSIONER BURNS: Thank you, Chairman, and thank you all for being here and the work that you do with the Committee. And Dr. Palestro and Ms. Weil, thank you for your services as you rotate off the Committee, I appreciate that.

You touched on a number of interesting topics this morning. Maybe I can start on the question on the authorized users. I appreciate that analysis, that data analysis.

One of the things I think we would get as Commissioners when we've had drop-in visits or other letters or information on the question on the authorized users was, and I think in a way Ms. Weil touched on it, is the question of access.

While I think statistically what you're showing, Dr. Metter, is that there is a pipeline or a refresh in the system, the question that some will raise is that may look fine as a generic matter if you look at it overall, but you may have regional issues with that or access in rural areas and things like that.

I don't know if you'd like to comment on that?

DR. METTER: The issue of rural areas and entities, they're not in the urban areas where they have the medical specialty, I=d like to make an analogy with chemotherapy.

So, as far as you have a specialist who can administer chemotherapy or radiation, an oncologist, and they know what to look for and right now the newer agents are getting more and more complicated in their indications, their administrations, their toxicities.

And really as far as our current authorized users we have to learn more. So the idea is not to decrease the level of knowledge, it's actually you have to increase it. And actually, it's not only the knowledge base, but it's the experience. And if you actually look at the rural areas, you have individuals -- you can have, say, for chemotherapy, you have an oncologist and you have -- and I was in family practice so I'm not putting that down, but you have a family practitioner who can go ahead and say, well, I'm going to push this, this is number one, this is number two.

And the patient starts having problems. They don't know how to deal with that and you know, you really need an expert. And radionuclide therapy is really getting, like I said, more complicated. Another issue in the rural areas is cost. The cost of these radionuclides are very expensive. I mentioned 177-lutetium, the cost of that agent for one therapy is analysis $50,000 just to order it by the pharmacy and that's not the cost that the insurance has to pay.

And that individual is not just one dose, they need four therapies, so you're looking at like $200,000 just to pay for the cost of the radiopharmaceutical.

And then if that site does not have the facilities of safely delivering it for the patient, the staff, and the public, I kind of made a general look at what's the cost as you just said in an area, it's going to be over $100,000.

And then you have to maintain it with the personnel and all that. And so in the rural area, yes, there's nothing that's going to stop them, it's going to be a financial issue.

And if you just have one or two insurance that doesn't pay for

it, it'll be not financially feasible for that community.

COMMISSIONER BURNS: Thank you. Dr. Ennis? Certainly.

DR. ENNIS: Just to add, the specialists who now have the main pathway training are nuclear medicine and radiation oncology who do things beyond radiopharmaceutical therapy, nuclear medicine, particularly mostly imaging, radiation oncology using external radiation treatments.

And there is no evidence or call from any sector of society that I know of a shortage of imaging availability in nuclear medicine or radiation oncology and external radiation.

So, how could that be that we have adequate supply even in the rural areas of radiation therapy, external treatments and nuclear medicine imaging? These are the same people.

So, it doesn't seem a logical or reasonable argument to think there really is an actual shortage of authorized users because these companies are being served by the other practices that these physicians provide.

It doesn't seem likely that they're there.

COMMISSIONER BURNS: Thank you. In some ways I guess it's related or it's a corollary area what I'm interested in.

I know this issue for example on training and either you have the certifications or then the provisions that include the 700 hours training. And that's another one over my term here that that issue has been raised.

Are you also looking at the issue overall on the 700 hours or the content or things like that, or what the training mods are?

DR. PALESTRO: The answer is at the present time no.

We have the Subcommittee on Training and Experience

which tends to go through all of the various training experience for all modalities and it was our plan to begin and work our way up for the 100, 200, 300 series and so forth.

However, we were directed to focus on the 390 series for the limited scope authorized user. So, the short answer to your question is it's not being done at the moment. We will get there in the future to look at the 700 hours.

COMMISSIONER BURNS: Okay, thank you. Dr. Metter?

DR. METTER: Yes, and one other major important thing regarding your question is that when you look at the overall spectrum of what that entails, the bottom line is it's not safe.

It's not safe for the patient and the public for the limited scope pathway.

COMMISSIONER BURNS: Okay, thank you. Dr. Ennis, I thought it was a very interesting presentation on this analysis of the medical events and the timeout or take a breath, it's sort of the same thing.

So I was very interested in the Committee's recommendation that the staff go forward in the information notice. This is probably not so much a question but I would hope the staff -- you all made the recommendation last September.

I think I probably would be interested to know, which is not something within your camp but from the staff as an outcome of this meeting, what's the resource hold-up and where we can move forward?

Because it's very interesting when you look at the statistics. Again, as you say, you're in a context of thousands and thousands of events with relatively few, which speaks well to I think the practice.

But still, there are instances where the learning is have I got the right person, have I got the right dose, have I got the right machine? Or whatever type question it is. So I found that extraordinarily interesting.

I don't know whether you looked at all -- within the set of a medical event, obviously some of those hit our Congressionally required targets for abnormal occurrences and I don't know if there was any particular focus on those within that set?

DR. ENNIS: Right, those are very rare and it was not a focus, it was not a specific focus.

COMMISSIONER BURNS: Okay, thanks. And Ms. Weil, in a sense related to your comments in terms of approving the NMED system, what would you say a vision for that in terms of making it maybe more broadly useful?

As you say, in many respects it helps the regulatory process or it's focused on that. Elaborate on what you were trying to tell us?

MS. WEIL: Sure. So, the cases that are entered into NMED are often incomplete and the information that would be useful for learning from a medical event is simply not accessible.

Perhaps the corrective actions haven't been entered or the description of the event is simply entered from a pick-list of menu items, which isn't -- there needs to be a narrative feel to describe what happened.

And then an evaluation of why it happened, and then an evaluation of what could one do to prevent it from happening again. Once those cases are complete and useful, then it should be accessible to the broader medical community.

It's not, you can't look into NMED unless you're authorized to

do so. And I don't know what the criteria are for getting into NMED, I know I can, but I know that the local physician in the hospital down the road can't.

And that's crazy, it should be available so that medical professionals can look at what happened to their colleagues and figure out ways not to have that happen to them.

COMMISSIONER BURNS: Anybody else care to comment. Dr. Ennis?

DR. ENNIS: Well, to that end, just to let you know, we do have a Subcommittee in ACMUI looking at this very question and it was an outgrowth of the first presentation I gave you.

So, we're not ready yet to make formal recommendations but we will have some ideas coming forth.

COMMISSIONER BURNS: Okay, great. Well, thank you again to all of you for your presentations and for your service on the Committee.

CHAIRMAN SVINICKI: Thank you very much. Next we will recognize for questions Commissioner Caputo. Please? I'm sorry, you can tell we had a Congressional Hearing this week. Commissioner Caputo, thank you.

COMMISSIONER CAPUTO: I've always got to stand up.

COMMISSIONER BARAN: We know who you are.

COMMISSIONER CAPUTO: I know who I am too. I'm certainly very aware I'm not a Senator. So, I'm going to start with sort of a broad forward-looking question for any of the panelists I think.

There was mention to increasing number of new therapies being developed. Are there any technologies or therapies that are under development that might require us to change our procedures or change our requirements?

Are there advances that we need to think of and be preparing in advance if they're going to require different means of regulation?

DR. PALESTRO: The answer is there are numerous new technologies as well as radiopharmaceuticals under development that we need to be aware of and when the time is appropriate, to focus on them and to make a determination about what sorts of procedures or training and experience need to be adjusted or modified.

And again, going back to the Training and Experience Subcommittee, while the focus has been for the past couple of years, and rightly so, on the limited authorized user status, that Committee was set up to be an ongoing Subcommittee and to keep abreast of these sorts of changes, review the various technologies, the various agents and so forth on a regular periodic basis and make recommendations from changes in Training and Experience.

COMMISSIONER CAPUTO: So, in general, in the past, have our regulations been flexible enough to accommodate new therapies coming into the market? Or in general, do we require tweaks?

DR. PALESTRO: I think that up until now, the regulations have been broad enough and comprehensive enough that there have not been issues with the introduction of new technologies.

Whether or not the current rules and regulations, training and experience and so forth, are going to be sufficient for the future, I don't know. I don't have an answer for that.

COMMISSIONER CAPUTO: All right, thank you. Dr. Metter, on nursing mothers, you mentioned that you think there needs to be signage to inform nursing mothers.

I've got to tell you, I think if I was in the position where I was a nursing mother and needing treatment, I would probably be thinking about so many things between worrying about my child and worrying about the threat to my life that I'd be a little distracted I would expect.

Isn't there a requirement for the folks that are administering the treatments to ask? Because there are any number of things that can be done to women where they will ask you five times, are you sure you're not pregnant? Yes, I'm sure.

Are you sure you're not pregnant? Yes, I'm sure. No, are you sure you're not pregnant? I mean there's such a thorough focus on that, isn't there a protocol for that?

DR. METTER: Well, for radionuclide therapy, in our institution anyway, I can't speak for other institutions, we meet the patient first and generally well in advance of the therapy.

And first of all, we go ahead and review the therapy to see if it's appropriate and if it's not appropriate, we contact the healthcare provider.

And if we find out the time that -- let's say there is a nursing mother when they come in, we then -- and I've done that before. I say I'm sorry. And most of their treatments are elective so there's time that we can go ahead and we educate the patient, and I had them come back in six weeks to be sure they're not lactating, and then I went ahead and treated her.

But, no, we do meet the patient, we take a history, we examine the patient, we discuss the procedure at length, and they come back generally for the procedure.

COMMISSIONER CAPUTO: But you said this protocol exists at your facility so it's not across the country? This isn't just standard protocol to

identify nursing mothers in advance of treatment?

DR. METTER: The practice of medicine is individually and is, as far as individual practitioners -- let's say if I were and like I said, I was in family practice, my way of treating of hypertension is very different than let's say Dr. Palestro's would be.

So it's something that we have to get out there and I think I actually make our clinicians know that.

COMMISSIONER CAPUTO: Okay, and that would be done through the information notice?

DR. METTER: That would be very helpful. And I think part of this is really your practitioners and we are in our own little world and we see our own little world as far as nuclear medicine, radiology. And we should actually, and this is a very good point, reach out to our primary care physicians or OB-GYN doctors and all those other societies to let them know this is available and this is an important issue regarding radiation to the nursing mother and child.

COMMISSIONER CAPUTO: All right, thank you.

Dr. Ennis, with regards to Yttrium-90, you mentioned residual activity remaining in the deliver device. What happens to it when it remains in the device?

Are we just talking about an inadequate dose to the patient? Does it end up located somewhere in other tissues that it was not intended? Or are there other complicated --

DR. ENNIS: There are different kinds. The issue within the treatment device just means it was not in the patient. And so it gets disposed of properly. There was no evidence of disposal issues or anything like that.

Just as an example, one problem can be a kinking of the tubing. The tubing is rather delicate and it may not be able to be unkinked so then there's a decrease and that leads to the medical event, because of a decreased dose compared to what was intended because of that.

COMMISSIONER CAPUTO: And of course, it's probably hard to determine exactly how much or too small the dose was.

DR. ENNIS: No, generally you can figure out the volume and therefore figure out what the dose was, and therefore you can determine whether it's reportable or not. But that's the issue.

COMMISSIONER CAPUTO: Actually, I have no further questions so I'll just turn back my time.

CHAIRMAN SVINICKI: Thank you very much. Next we'll heard from Commissioner Wright. Please proceed.

COMMISSIONER WRIGHT: Thank you, Madam Chairman. I'm so happy you're back here so we could have celebrated with you today.

We did miss you last week and congratulations to both of you, we'll be missing you. And thank you for your service.

So, a couple of softball questions, Dr. Palestro. The interaction with the NRC staff, are you getting what you need? And how are things going I them?

DR. PALESTRO: The answer is I've been on the Committee now for eight years and the interactions have always been cordial, prompt, through, informative, and I think mutually beneficial.

And I think it should be pointed out that for nearly two years we were without an ACMUI coordinator, and I don't think I realized how much work that individual did until they were no longer there.

But in that individual's absence, that position was more than competently and admirably filled by Ms. Sophie Holiday, Ms. Lisa Dimmick, and Mr. Doug Bollock, as well as the remainder of the staff.

So the answer is that was an unfortunate incident but they more than compensated for that vacancy over what was a fairly long time.

COMMISSIONER WRIGHT: Thank you for that and I'm glad you recognized my name. That really is important so thank you.

So, I guess what do you foresee as a medical -- in the community, what's going to rise up to the level that maybe the NRC needs to be prepared for going forward with new emerging technologies or anything like that?

Can you maybe give me a little insight?

DR. PALESTRO: I think certainly from the nuclear medicine standpoint, which is my area of expertise, therapeutic agents, they have been slow to develop over the years but there seems to be an increasing number of them coming at a more rapid pace. For example, we've talked about lutetium-177 dotatate, which was approved I guess about two years ago. But there was another agent, I-131 MIBG designed to treat certain neuroendocrine tumors that was approved this past July.

There are other therapeutic agents still not approved for prostate carcinoma and for some other malignancies that will undoubtedly be available in the near future. Their administration is a bit more complex in many cases than what we've had in the past. So the knowledge of the individuals administering them will have to be more comprehensive than it was in the past.

I'm not an expert on radiation oncology and that technology

and with your presumably, sir, I would defer to Dr. Ennis who I think is in a better position to answer that.

COMMISSIONER WRIGHT: Sure.

DR. ENNIS: So there are always to me a remarkable number of creative people out there coming up with new ways to apply radioactive materials and there are a number of devices that have been developed or are under development.

I do not foresee them creating challenges for the NRC, the structure that's in place. As best I understand, everything that's in development would fit within the structure and be able to be handled appropriately there.

The challenge for them is a little bit outside of the regulatory space but still within NRC's space if you will.

There are some forces at play trying to discourage radioactive material usages and I do have a concern that that will decrease innovation over time to the detriment of patients.

So, that's more of I guess a political issue than a regulatory one, but still one that NRC plays a role in. And I hope we'll be able to continue to develop these.

COMMISSIONER WRIGHT: Thank you. So I'm going to take a little different track because having been the recipient as a colon cancer patient, and my daughter as well, Stage 3C, so we've gone through that.

So I understand the importance of the people who are going to be treating you having the knowledge and the skillset and the repetition of have them doing it for the safety of myself as a patient and my daughter as a patient and anybody else who is a patient. Because it's critical.

So, I recognize what you're saying and I believe I understand

you've already answered Commissioner Burns' question about what your challenges were and why you have the position today that you did, which I guess is a little different than last year a little bit.

You've come out in a little stronger position now, and I understand it. I want to go to access a little bit because you brought up insurance and with an patient advocate here too, I'm from South Carolina.

We are a very rural state, we're a very poor state, access is an issue. We have many, many people who are uninsured or under-insured and we're not unique in that as a state, probably more in the Southern states than anywhere else around the country. So, to the point that there are also poorer people if they don't have insurance so they can't go get screened, for example. They can't take the time off if they have a job.

They have to take two days off and that's to them a lot of money so we're trying to find ways to help them. How do you address that if we have someone who is uninsured?

For example, I don't know, they're playing Russian roulette with their life to go get screened or not. And then if they're found to have cancer then they have to go into a situation where they have to receive radiation or any other type of therapy, what if they're uninsured? How do you handle that?

Is that something you can kind of give me something about? Because I hear what you're talking about, but that's people who have insurance. How do the other people -- and how do you handle that?

Because I know you're caring people. So just if you could give me a little bit of background for that?

MS. WEIL: Well, healthcare is not a right in the United States

and access is based on your ability to pay. Most institutions do have charity care and there are ways of receiving care if you can get to the institution but that's not something that the NRC can fix.

COMMISSIONER WRIGHT: Right, I understand that. But you say there's not a shortage and I agree with that. But if you're going to be treated, you've got to go to a facility that may be out of your ability to get to.

And I know there's data that really supports where they're at and I know it's a financial decision too, whether you're going to put that stuff in the community or not.

So, I'm trying to understand and get a balance about that myself for the access part of it.

MS. WEIL: If I can just take it a little further, Dr. Metter used an analogy and I=d like to use a different analogy.

In the rural community medical center or just in a rural community in general, there may not be a pediatric neurosurgeon. And surgeons are not suggesting that general surgeons in rural companies or surgical PAs should be licensed to perform pediatric neurosurgery.

It's not a matter of access, it's a matter of expertise and appropriateness, and some people don't live near what they need. But one shouldn't compromise safety in order to provide access.

COMMISSIONER WRIGHT: Exactly. Thank you for that.

DR. METTER: And I=d like to actually expound on that. I did mention safety in Dr. Ennis' report with medical events and these are individuals who are highly trained.

One-third medical events was related to infrequent use so that's one out of three. So I think the expertise is really important and if were

giving your family, your child, any procedure or anything, you'd want it to be done by the best person you can do.

And so I know it's an unfortunate thing as far as Ms. Weil -- we did promote her by the way. I'm here today because I care about patients, that's why I went into medicine and I want to do the best for my patients.

And I think safety is a very important issue and I think as regulators, that's our goal.

COMMISSIONER WRIGHT: Great, well, thank you so much. Thank you.

CHAIRMAN SVINICKI: I will maybe continue some themes that my colleagues have begun. But I did have a point of clarification.

First, Dr. Metter, on your Slide 22 and continuing on 23, you had nursing mother recommendations for those instances where a nursing interruption would be sufficient and you didn't need to have total cessation.

I was just curious about the durations that were listed here. How would you characterize the sense of medical certainty around the sufficiency of these durations? Are they a minimum duration for interruption? Would it depend on the biology of the individual lactating mother? Or is this fairly settled in terms of these recommendations, like there's a lot of concreteness around them?

DR. METTER: The individual who actually did the calculations was Dr. Zanzonico. He's actually one of the leading experts on this in the country and there's actually a very complicated formula and physics involved.

And these are the requirements for the safety of the mother and the lactation state, it doesn't matter. The only one that really matters is the

I-131.

CHAIRMAN SVINICKI: Okay. That's actually very helpful. I was a little surprised not to see them maybe as a range or something like that given the complexity of it as you've just acknowledged.

DR. METTER: And so the other thing we look at something called half-life and that's actually very standard as far as the physical half-life. But you're right, the biology is going to be different. So really, these are the maximum so we actually went the most conservative so these would be the maximum. So, you might fall within let's say it's seven days or you may fall in the three days but we say seven days.

And so this is the maximum for the patient safety.

CHAIRMAN SVINICKI: Okay, I thought it was probably something along those lines because you'd need to have a conservatism in there. Dr. Palestro, did you want to --

DR. PALESTRO: Yes, Madam Chair. In addition, the objective was to make the guidelines as uncomplicated for those of us who have to issue them as well as for the patients.

If we were to say three to seven days you should refrain from breastfeeding, it's a lot more of a decision placed on the patient than to say seven days no breastfeeding.

So, we took a very conservative approach and tried to keep it as simple as possible while maximizing safety.

CHAIRMAN SVINICKI: Thank you for that and I think there is merit if you're going to go out with the guidelines to try to make it straightforward.

And if you're going to do that then you would error on the side

probably of the more conservative and longer duration for the interruption. Thank you. That was a helpful clarification.

And then on the issue of the potential recommendation for the timeout, I appreciated the multi-year evaluation, Dr. Ennis, of the medical events.

As you noted, there are so few per year, which is of course a good news thing, but I think it's useful to try to look across years. I think in any given year it would be really difficult to reside a lot of confidence across a population of events so small.

And again, the denominator is so overwhelmingly massive in comparison to the event. As I was listening to the timeout concept, I was thinking about the nuclear industry as a whole which often before some sort of modification of something in a nuclear plant is undertaken, they do what they call a pre-job brief.

It's the team that will be conducting whatever they're about to do. Of course, it's been trained, has read the procedure, but it is to say we're gathered here to do this now and let's all agree that we understand what the steps are.

And is this the right pump that we're about to open up and modify? Things like that. So, you mentioned that something a kind to a timeout is often found maybe in operating theaters or a surgical context or something like that, so my question was is this kind of a current best practice?

And how much of a change in procedure would it be to implement that more broadly in the radiation and radiopharmaceutical techniques?

DR. ENNIS: So I think that it has been implemented in some

practices but it's clearly not in others, just from experience and clearly from some of the events.

So, these kinds of concepts are infiltrating into medicine at large.

CHAIRMAN SVINICKI: Okay, thank you. And then another aspect of the categorization of events or causes was the infrequent user, and that pointed out to me I have a lack of awareness.

My sense is that practitioners in this field of expertise specialize a bit -- this is a really difficult question to phrase intelligently.

But is it somewhat uncommon for a practitioner to be asked to do something to administer a technique of some kind that would be truly infrequent, like once a year?

Is there kind of a specialization that occurs amongst the practitioners?

DR. ENNIS: I think it's hard to really --

CHAIRMAN SVINICKI: Characterize --

(Simultaneous Speaking.)

DR. ENNIS: -- characterize this.

I would say that getting back to Commissioner Wright's comments, it certainly could happen and does happen that if I'm in a relatively small rural practice perhaps I'll have only one cervix patient a year who needs an implant.

And even though I trained and did lots of them when I trained, if I'm my age now and I've only been doing one a year, maybe I need a refresher before I do each one, for example.

CHAIRMAN SVINICKI: Okay, that's helpful. Does any other

Member of the Committee have just a broad perspective on how frequently a practitioner is confronted with doing something they do very, very rarely?

Is that a good broad characterization that Dr. Ennis has given, that it can happen, it does happen depending on where you're practicing?

MS. WEIL: I think with the introduction of limited scope licenses, it's more likely to happen more often because you wouldn't be serving patients in Centers of Excellence where things happen all the time, but rather in smaller practices.

CHAIRMAN SVINICKI: Okay, that's helpful. Dr. Metter, did you want to add to that?

DR. METTER: Yes. So, when you actually look at radionuclide therapy, and I mentioned before, there's a certain basic minimal level of competency you must master.

So if you have those basic tools, if something comes up that you've already been trained for like Dr. Ennis, you know what to do and you know to look for flags and look for any adverse issues that occur or toxicities.

So, you have to still have the basic knowledge topic, and the frequency issue is a problem but you're trained to look for that and take care of it. And then also, continuing and refreshing up on reviewing the therapy before you perform it.

CHAIRMAN SVINICKI: Okay, thank you, that's helpful. And in your responses you kind of got to the kernel of why the question matters, which is that is this something that isn't common and we don't need to worry about?

Or with again potential new modalities and treatments coming out, could this be actually a cause, a possible systemic cause, of medical

events that is actually growing in its incidence so that you would want to put measures in place?

Dr. Palestro?

DR. PALESTRO: Yes, just adding to that, there's no doubt that the more frequently an individual performs a task, excuse me, the more proficient they are at it.

And we tend to focus on rural areas as potentially being underserved or having less access. I think it's equally important to point out that there are small or smaller community hospitals that are not in rural areas in which these types of procedures are practiced only infrequently.

And you can say, well, you're only 50 miles from Manhattan and you've got some of the greater hospitals in the world, why don't you go there?

And the answer is patients I think inherently are more comfortable with going locally, and so it's not something that's limited just to rural or underserved areas.

CHAIRMAN SVINICKI: Well, thank you for that point.

And to build off that, it's not so much a question but some of my colleagues have asked questions about access and I find, Ms. Weil, I appreciated your acknowledgment of an evolving perspective on the development of alternative pathways or other standards for the training and qualification of practitioners who might administer things.

In the course of thinking about this over the years myself, you're confronted with the developers of new modalities and things that come in and say, well, it would just be in some sort of thing that is already prepared in the dosage and it's so portable and injectable.

But what began to weigh heavily in my mind is something that you all have commented on, which is the individual biology of any given patient and how they might react to something, and the broad base of both knowledge of that patient and medical background that's necessary should their individual reaction to something not be exactly what was predicted.

Each patient falls somewhere on a continuum of how they tolerate something or complications or other things going on. And while access is something that certainly would bring cost down and would proliferate the availability of techniques to patients who might benefit from it, there is this overriding safety benefit, greater access if it comes at the expense of greater risk to the ultimate patient care.

And again, as we were mentioning with the lactating mothers, there's individual biology and what's happening and the individual health status of each of the people receiving this.

And so while they want access, should they not also benefit from having the kind of care provider that would know the totality of their medical circumstance?

And maybe have a better sense of how their individual system is going to react to anything that is administered.

I know that falls in the category of unknown unknowns and that can't by itself be a reason why there are significant obstacles to something, but I think, Ms. Weil, as you mentioned in your statement, it is something that needs to be given considerable weight here as we move forward.

And with that, I just wanted to close by stating that I have been so impressed over the course of time with the thoughtfulness you've brought to the balancing of factors, as I call it. It's kind of a term that

decision-makers use.

But often in complex issues where there are a lot of important public goods or public health objectives to be met, we have to balance a lot of different factors.

I have noticed I have no training in medical ethics or ethics generally, I'm an engineer so we didn't have a lot of time for those types of topics while interesting.

But as the Committee thinks about filling your big shoes behind you, I do think that someone who had a formalized training, I've watched you balance a lot of ethical factors and it is a complex art all in itself. And it is a skill area and there are people who specialize in it.

And so I'm not saying that the patients' right advocate should become a medical ethicist but I think there's merit to thinking about as we look at candidates, if candidates come forward that have that. I've benefitted from it as I've thought about these issues so I don't know. I'm over my time but if you wanted to add anything to that?

MS. WEIL: I think it's a useful framework for looking at advocacy issues, but then there are many useful frameworks. And I know that my seat on the Committee is a hard thing to fill, but I agree with you it's useful.

CHAIRMAN SVINICKI: Okay, thank you very much. And with that, we will turn to Commissioner Baran.

COMMISSIONER BARAN: Well, thank you for your presentations and for all your work. I think the discussion on the Training and Experience requirements has been good. I have a few additional questions there.

It sounds like a significant factor in the Committee's

conclusion that we should stick with the 700 hours requirement and not go down the path of a limited scope authorized user for particular radiopharmaceuticals or classes of radiopharmaceuticals.

It sounds like a key factor or a significant factor in that analysis. It has to do with the toxicity of some of the emerging therapies and risks associated with misadministering some of these radiopharmaceuticals.

Can you talk a little bit more about that? Has there been a change? Is there a difference in the toxicity of the newer therapies than previous therapies?

How does all that factor into your thinking?

DR. METTER: So one of our earlier therapies, as you know, is I-131 for thyroid disease. And so that in itself is one organ and the goal of the therapy generally is to destroy disease tissue. So, that was one item.

The next one is that that became more available, there was Zevalin for a little time but that passed. And then now we have Xofigo, our alpha agent for bone metastases.

Now, that's a little more complex. We don't want to destroy all the bone, okay? We want to just destroy the disease but that in itself becomes more complex although it's still one organ.

Lutetium-177 has come out and that's a neuroendocrine tumor which you could have multiple types of tumors in multiple different organs.

And then it's a very complex administration, it usually takes half a day or longer because there's toxicity to the kidneys so we have to protect and some special protection with that.

And then you have a lot of nursing staff and it's a really a

team of people, as opposed to the others before. You have your patient and your technologist and it's a very limited group.

Now it's a bigger area, you have to have special rooms and things like that. So, yes, it is becoming more complex and so that opens the door with lutetium-177.

COMMISSIONER BARAN: And so with that complexity, if I understand the presentation right, when you look at the training topics, a limited scope authorized user should have a particular radiopharmaceutical or class of radiopharmaceuticals. You end up with a list that's basically the same as what you would have for the 700 hours for a full-blown authorized user when you did that analysis?

Is that the right way to think about it?

DR. METTER: Are you talking about lutetium?

DR. ENNIS: No, just in general, yes. Concluding that when your Committee tried to look at what would be required for a limited scope license it was practically the entire curriculum. And then when you looked at another class of isotopes, you came to the same conclusion.

So you concluded there really wasn't room for a limited scope license because the broad knowledge you need even to do one of these is essentially the whole curriculum.

DR. METTER: Because each radiopharmaceutical has their own complexity and once you look at it they all kind of overlap.

And when you look at it, it would just be the same training requirements for radionuclide A and B, and so it doesn't seem feasible to separate things out with the same training requirements and call them different things.

And so that was the main basis of that.

COMMISSIONER BARAN: Ms. Weil, did you want to...?

MS. WEIL: When we looked at 700 hours we were actually very uncomfortable with the concept of hours because we really wanted to assure that there were certain competencies.

And if we had the time and the resources, we'd probably want to come up with competencies rather than hours. But as a surrogate, hours work but that's not what it's about.

It's knowing that a provider is competent in the areas that are required.

DR. METTER: I believe I misunderstood your question, but yes, our Committee is actually looking at the knowledge topics that you need to know. And really the bottom line is everybody is a different learner, but at some point in time you have to end up with hours because that's how you have to adjust things.

But right now we're looking at what is the basis for the future as far as other items that an individual needs to know? And then really the bottom line is going to be the competency assessment.

You may know these knowledge topics but can you apply them? Can you use them? Can you use them safely? And that's going to generally be through a certification exam.

And again, in my topics I mentioned that it's not only a certification which occurs one time. And in the past you understand we used to have Board certification and you're forever and then they had recertification every ten years.

And now they're going into ongoing longitudinal assessment

with recurring further questions reassessments.

And so I think that's going to be very important to maintain your competency and that's going to be best for the patient. And especially like we mentioned with emerging technologies and new radiopharmaceuticals.

COMMISSIONER BARAN: Okay, and so I guess in my mind I was kind of having a close nexus between the 700 hours and whether we should pursue some type of limited scope authorized user.

It sounds like you all are still looking at the question about whether 700 hours itself makes sense as the authorized user requirement. Is that right?

Or whether it makes sense to move to something more competency-based, whatever that would look like?

DR. METTER: We're working on that, yes.

COMMISSIONER BARAN: So that piece is still ongoing.

I saw that one member voted not to approve the final Training and Experience report and I was just wondering whether someone's able to discuss or represent whatever the area of disagreement was there?

DR. PALESTRO: I was the dissenting Member on that Subcommittee and the former Chair of that Subcommittee. My concerns are as follows.

Number one, we've seen a documentation of the number of authorized users that are available and the conclusion was that this is a sufficient number. The problem that I have is on what data is that conclusion based?

I can't tell you that it's incorrect but I can't tell you that it's correct. I didn't see any data that says there should be or it's estimated that

there should have been 1 AU per 100,000 people or per 1 million people and so forth.

So, I'm not willing to accept that as fact, that there are sufficient numbers of authorized users.

My concern, as I've expressed in the past, is that as these new agents are developed and as there is presumably going to be an increased demand for their use, will there be a sufficient benefit of authorized users?

And again, I don't have an answer for that. And rather than being reactive in the future when we suddenly say, wow, we are short, we need to develop more authorized users, I would rather be proactive and have an alternative pathway established. And the reason why I want to be proactive is because it takes a long time to be able to, at least as far as I know, get these programs into place. So rather than waiting until such a time as a crisis is developed and then saying, well, now it's going to take us five or six or seven years to ramp up the manpower, be prepared ahead of time.

Do I think that's going to solve all of the problems in terms of access? No, not in and of itself because the long and the short of it is that there are areas, and they don't have to be rural, that people simply aren't interested in going to for one reason or another and have never been interested in going to.

And those areas will always have manpower shortages, and there are other ways around that but that's beyond the scope of what we do.

So, again, I haven't changed my philosophy and my opinion, I still believe that we should be proactive rather than reactive and I would like to see an alternative AU program in place.

I'm also not convinced that it has to be identical to the current alternate pathway because much of that pathway pertains to diagnostic

procedures.

And I'm unwilling to put a number of hours on it because I've been opposed to hours from the beginning, and it would be focused on competency.

COMMISSIONER BARAN: Thank you for that. And just have a little bit of time left but earlier this year, the final rule, the Part 35 rule, which made several changes to the regulations related to the medical use of byproduct material took effect.

I'd just be interested in any brief thoughts you all had about how the implementation of those changes has been going. Does anyone have any early perspectives to share on that? If not, that's fine too.

Okay, that's fine. Thanks.

CHAIRMAN SVINICKI: All right, thank you very much. Again, my thanks to the Committee and to my colleagues. Again, I think the discussion made clear the wonderful benefit of having this Committee's perspectives available to Members of our Commission. So, thank you for that and I will adjourn us but I think that we are scheduled to do a photo so I would ask that you Committee Members not dash out of the room super quick. We can just get it over with really fast if we all stay in the room.

Thank you and we are adjourned.

(Whereupon, the above-entitled matter went off the record at 11:42 a.m.)