Official Transcript of Proceedings

NUCLEAR REGULATORY COMMISSION

Title: Meeting of the Advisory Committee on the Medical Uses of Isotopes

Docket Number: (n/a)

Location: Rockville, Maryland

Date: Monday, April 8, 2024

Work Order No.: NRC-2751 Pages 1-201

NEAL R. GROSS AND CO., INC.
Court Reporters and Transcribers
1716 14th Street, N.W.
Washington, D.C. 20009
(202) 234-4433

UNITED STATES OF AMERICA

NUCLEAR REGULATORY COMMISSION

+ + + + +

ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

+ + + + +

TELECONFERENCE

+ + + + +

MONDAY,

APRIL 8, 2024

+ + + + +

The meeting was convened via Videoconference, at 8:30 a.m. EST, Hossein Jadvar, ACMUI Chairman, presiding.

MEMBERS PRESENT:

HOSSEIN JADVAR, M.D., Ph.D., Chairman

RICHARD L. GREEN, Vice Chairman

ANDREW EINSTEIN, M.D., Member

MICHAEL R. FOLKERT, M.D., Ph.D., Member

RICHARD HARVEY, DrPH

JOSH MAILMAN, Member

MELISSA C. MARTIN, Member

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

ZOUBIR OUHIB, Member

MEGAN L. SHOBER, Member

HARVEY B. WOLKOV, M.D., Member

JOANNA R. FAIR, MD, Ph.D., Member

NRC STAFF PRESENT:

CHRISTIAN EINBERB, Designated Federal Officer, NMSS

KEVIN WILLIAMS, NMSS

CELIMAR VALENTIN-RODRIGUEZ, NMSS

LILLIAN ARMSTEAD, Designated Federal Officer, NMSS

CYNTHIA M. FLANNERY, NMSS

MARYANN AYOADE, NMSS

DANIEL DiMARCO, NMSS

VINCE HOLAHAN, NMSS

DANIEL SHAW, NMSS

KATHERINE TAPP, NMSS

SARAH SPENCE, NMSS

KENN BRENNEMAN, NMSS

Vincent Holahan, NMSS

C-O-N-T-E-N-T-S

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

8:32 a.m.

MR. EINBERG: Okay. Good morning. I have a little bit of echo. Is the court reporter on? If you're on, the court reporter, can you please let us know, please.

COURT REPORTER: Hi, good morning.

MR. EINBERG: Okay, thank you so much. So, we'll go ahead and get started. Good morning. As the designated federal officer for this meeting, I am pleased to welcome you to the public meeting of the Advisory Committee on the Medical Use of Isotopes.

My name is Chris Einberg. I am the chief of the medical safety and events assessment branch, and I have been designated as the federal officer for this advisory committee in accordance with 10 CFR Part 7.11. This is an announced meeting of the committee.

It is being held in accordance with the rules and regulations of the Federal Advisory Committee Act and the Nuclear Regulatory Commission. This meeting is being transcribed by the NRC, and it may also be transcribed or recorded by others. The meeting was announced in the March 7th, 2024 edition

of the Federal Register, Volume 89, page 16590.

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

I request that whenever possible we try to reach a consensus on the various issues that we will discuss today. But I also recognize there may be a minority or dissenting opinion. If you have such opinions, please allow them to be read into the record. At this point, I would like to perform a roll call of the ACMUI members participating today. Dr. Hossein Jadvar, Chair, Nuclear Medicine Physician.

DR. JADVAR: Present.

MR. EINBERG: Mr. Richard L. Green, Vice Chair, Nuclear Pharmacist.

MR. GREEN: Present.

MR. EINBERG: Michael R. Folkert, Radiation Oncologist.

Michael R. Folkert: Present.

MR. EINBERG: Mr. Josh Mailman, Patient's

Rights Advocate.

Mr. Josh Mailman: Present.

MR. EINBERG: Ms. Melissa Martin, Nuclear Medicine Physicist.

Ms. Melissa Martin: Present.

MR. EINBERG: Dr. Michael O'Hara, FDA Representative.

DR. O'HARA: Present.

MR. EINBERG: Mr. Zoubir Ouhib, Radiation Therapy Physicist, and he's participating virtually. Are you online?

Mr. Zoubir Ouhib: Present.

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

MS. SHOBER: Present.

MR. EINBERG: Dr. Harvey Wolkov, Radiation Oncologist.

DR. WOLKOV: Present.

MR. EINBERG: Dr. Richard Harvey, Radiation Safety Officer.

DR. HARVEY: Present.

MR. EINBERG: Dr. Andrew Einstein, Nuclear Cardiologist.

DR. EINSTEIN: Present.

MR. EINBERG: Dr. Joanna R. Fair,

Diagnostic Radiologist.

DR. FAIR: Present.

MR. EINBERG: I confirm that we do have quorum of at least six members present. Ms. Rebecca Allen was unable to join us today. However, we'd like to welcome Dr. Fair as this is her first meeting as part of the ACMUI.

She has been selected as the diagnostic radiologist representative. Dr. Fair is pending her security clearance but may participate in today's meeting and is welcome to comment and ask questions at the appropriate time. However, she will not have voting rights for any actions requiring a vote.

All members of the ACMUI are subject to federal ethics laws and regulations and received annual training on these requirements. If a member believes that they may have a conflict of interest as the term is broadly used in 5 CFR Part 2635 with regard to an agenda item to be addressed by the ACMUI, this member should divulge it to the chair and the DFO as soon as possible before the ACMUI discusses it as an agenda item. ACMUI members must recuse themselves from participating in any agenda item which they may have a conflict of interest unless they received a waiver or prior authorization from

the appropriate NRC official.

I would like to add we are also using Microsoft Teams so that members of the public and other individuals can watch online or join via phone. The phone number for the meeting is 301-576-2978. Once again, that number is 301-576-2978. The phone conference ID is 954-210-683#. Once again, the conference ID number is 954-210-683#.

The handouts and agenda for this meeting are available on the NRC's ACMUI public website. Members of the public who notified Ms. Armstead that they will be participating via Microsoft Teams will be captured as participants in the transcript. Those of you who did not provide prior notification, please contact Ms. Armstead by email at lxa5@nrc.gov, lxa5@nrc.gov at the conclusion of this meeting.

Today's meeting is being transcribed by a court reporter. We are utilizing Microsoft Teams for the audio of today's meeting to view presentation material in real time. The meeting materials and agenda for this meeting can be accessed from the NRC's public meeting schedule.

For the purpose of this meeting, the chat feature in Microsoft Teams has been disabled. Dr. Jadvar at his discretion may entertain comments or

questions from members of the public who are participating today. Individuals who would like to ask a question or make a comment regarding the specific topic of the committee as discussed and are in the room can come up to either of the microphones set up on the right side over there by the podium.

For those individuals on Microsoft Teams, please use the raise hand function to signal to our Microsoft Teams host, Ms. Armstead, that you wish to speak. If you have called into the Microsoft Teams using your phone, please ensure you have unmuted your phone. When you begin your comments, please clearly state your first and last name for the record.

Comments and questions are typically addressed by the committee near the end of the presentation after the committee has fully discussed the topic. We will announce when we are ready for the public comment portion of the meeting. And Ms. Armstead will assist in facilitating public comments.

At this time, I ask that everyone who is not speaking to please mute your Teams microphones or phone. And for those in the room, please mute your phones. I will now turn the meeting over to Mr. Kevin Williams, Director of the Division of Materials Safety Security and Tribal Programs for some opening

remarks.

MR. WILLIAMS: Thank you, Chris. Good morning to those who are in the room and those who are on Teams. It's a pleasure to be here with you and I welcome the spirited conversations that we will have over the next few days.

I want to first begin by thanking ACMUI for all of your hard work, your dedication, and your support to the NRC. We truly value your contributions and expertise as we continue to tackle a number of new issues related to the medical use of radioactive material. I would like to highlight a few items that may be of interest to the ACMUI and those who are participating in this meeting.

The first one is reporting nuclear medical injection extravasations as medical events. The rulemaking that we are conducting, the staff is proposing rulemaking package to codify certain medical injection extravasations as medical events and 10 CFR 35.3045. Along with the proposed rule, the staff developed implementation guidance for the rule which includes regulatory guidance for all medical events including nuclear medical injection extravasations and a draft model procedure for detecting and evaluating nuclear medicine injection

extravasations.

The draft proposed rule is currently in concurrence and staff expects to provide the proposed package to the Commission in August of 2024. Related to this topic, on March 26, 2024, the Office of the Inspector General released a report where they document the appearance of a conflict of interest involving members of the ACMUI. The OIG received allegations that at the time that the ACMUI was advising the NRC on matters related to a petition for rulemaking, specifically 35-22.

Several ACMUI members who are affiliated with the Society of Nuclear Medicine and Molecular Imaging, SNMMI, and that relationship between these ACMUI members and SNMMI created a conflict of interest. In their report, the IG found that two ACMUI members did not follow the procedures as outlined by Chris earlier, personal, business, and did not follow those procedures related to personal and business relationships when these members were participating in matters related to PRM 35-22 without obtaining prior authorization to do so. The OIG also found that the NRC's policies to ensure compliance with 5 CFR 26.3502 would need to be revised.

The OIG found, however, that neither

member had a personal financial interest that would have been affected by the matters related to PRM 35-22. I want to recognize that -- I recognize that the NRC and the ACMUI takes their job seriously. They maintain the integrity of what they're trying to achieve, and they do it with the upmost integrity and I really appreciate that.

We do take this -- it is a decision-making process. But I have found that the ACMUI has demonstrated continued integrity in its decision making, particular regarding matters impacting public health and safety. The OIG investigation highlights areas where our internal processes led to questions about the integrity of our decision making.

We plan to update our procedures to ensure that we are upholding the public trust. We'd also like to highlight that extravasations rulemaking is informed by a balanced set of views well beyond what is cited in the OIG investigation having an apparent conflict of interest. Our staff's independent evaluation of the technical issues considered input from various stakeholders, including the petitioner, the ACMUI, the Agreement States, and published literature.

The evaluation led to the staff's plan to

require reporting of certain nuclear extravasations. The 12 member ACMUI unanimously supported this recommendation which underscores the validity of the staff's approach. Again, as I say, I appreciate the integrity of the ACMUI and look forward to continued engagement on items of medical interest.

Training and experience for unsealed byproduct material, the staff is developing implementation guidance for training and experience requirements as directed by the Commission. The draft implementation guidance will be issued in August of 2024 as interim staff guidance or referred to as an ISG and will address persons seeking authorized individual status under Part 35 can fulfill training and experience requirements as well as clarify the roles and responsibilities of those persons involved in and subject to training and experience requirements. Pending on the clearance, the ISG will be sent to the Agreement States for a 60-day review period.

The draft ISG is being reviewed by the ACMUI's T&E and for all modality subcommittee. A public teleconference will be scheduled for next month for the ACMUI's full committee vote on the subcommittee's report. Reg Guide 8.39, Phase 2 of

that, the staff is in the process of responding to public comment on the proposed Phase 2 revision to Regulatory Guide 8.39.

As commenters had concerns regarding the cost and complexity of the proposed regulatory guide, the staff is in the process of simplifying the guidance and expanding the original regulatory analysis to include a quantitative cost benefit analysis. The cost benefit analysis addresses concerns related to the cost associated with the proposed revisions to the methodology in Reg Guide 8.39. Once the staff develops its proposed revision and analysis, ACMUI will receive it for review and comment.

Organizational changes with the NRC since the fall meeting, we welcome one new staff member into the medical radiation safety team. And that is Mr. Aaron Thomlinson. Mr. Thomlinson was selected as a graduate fellowship for NMSS and will pursue graduate studies in medical physics within the biomedical engineering PhD program at the University of Texas Southwest Medical Center.

I wanted to also recognize that our EDO Dan Dorman retired in January along with Cathie Haney. And the NRC is in the process of replacing

those two individuals. Once that decision has been made, we will share that information.

Changes in ACMUI, Dr. Jadvar is now the ACMUI chair and Mr. Green is the vice chair. Since the fall meeting, Dr. Darlene Metter completed her second term in ACMUI, and her departure left a vacancy for the ACMUI diagnostic radiologist representative. And Chris earlier now said Dr. Joanna R. Fair has been appointed to serve in this capacity.

She currently serves as a senior associate dean of graduate medical education and designated institutional official and vice chair for the academic affairs in the Department of Radiology for the University of New Mexico School of Medicine. The following presentations will be discussed today. Mr. Dimarco will provide an overview of recent medical events. Mr. Harvey -- I'm sorry, Dr. Harvey will provide the ACMUI analysis of medical events from fiscal year 2022 to '23.

Dr. Folkert, Dr. Wolkov, and Mr. -- I'll say your name wrong, I apologize -- Ouhib will discuss their subcommittee's review of NRC's draft licensing guidance documents for three emerging medical technologies. Mr. Green will provide an overview of prescription air reduction methods. Dr. Valentin-

Rodriguez will provide an update on medical team's activities.

I thank you for the opportunity to open the meeting. I wish you a productive session today. I will be in and out myself, but I plan to be here until 11:00 o'clock. My wife has a doctor's appointment this afternoon that I will taking her to.

MS. ARMSTEAD: Hello, everyone. I am Lillian Armstead and this morning I'll be providing the old business report and giving a status and an update on some of the items from the ACMUI's recommendations and action items. Item No. 11 dated 9-21-2020, as part of the -- excuse me -- as part of the nonmedical events report, the ACMUI recommended to the NRC staff and MMP to evaluate the issue of detection of short-lived medical isotopes and municipal waste from nuclear patients that might be triggering the landfall alarms and provide some level of guidance and best practices for additional instructions.

This item is currently open with an anticipated completion date of fall 2024. Item No. 7, dated October 4th, 2021, the ACMUI formed a new subcommittee on the Liberty Vision Y-90 manual brachytherapy source. The subcommittee is expected

to provide a draft report and any recommendations at the spring 2022 ACMUI meeting.

We propose to close as the subcommittee will be presenting during this meeting. Item No. 10, October 4th, 2021, the ACMUI endorsed radionuclide generator knowledge and practice requirements subcommittee report and the recommendations provided therein. This item remains open with an anticipated completion date of March 2026.

Item No. 4 dated December 5th, 2022, the ACMUI endorsed a Y-90 microsphere ME subcommittee report and the recommendations therein. The item remains open with an anticipated completion date of fall 2024. Item No. 6 dated December 5th, 2022, the ACMUI established two subcommittees, one to create generic process checklist to be used during medical administrations and one to review the DFA draft proposed rule.

The ACMUI also reestablished nursing mother's guidelines to update the 2019 guidelines. This item remains open with an anticipated completion date of fall 2023. Item No. 1 dated November 23rd, 2024, the ACMUI tentatively scheduled the spring meeting for April 8th through 9th, 2024. We propose to close this item as the meeting is today.

Item No. 2 dated October 23rd, 2024, the ACMUI recommended the NRC obtain the number of annual Y-90 microsphere administrations from the manufacturers. We propose to close this item today during this meeting. Dr. Jadvar and staff, this completes the old --

MR. GREEN: Lillian, on Item 6, it had a target completion date of fall '23. Should that be revised? Is that a typo? Should that be fall '24?

DR. VALENTIN-RODRIGUEZ: Yes, so one of the subcommittees that was established was the decommissioning of financial assurance. That was completed and we'll close that. The generic process checklist subcommittee, now that the medical events subcommittee has done their biannual review, we're proposing to expand the charge of that subcommittee to address that. And then for the nursing mothers' guidelines, since we're going through the revision of Reg Guide 8.39, we were looking to expand the charge on that -- reestablish that subcommittee to address that. So yes, those will hopefully address by fall 2024.

MS. ARMSTEAD: Dr. Jadvar and ACMUI staff, this completes the old business report and review of the ACMUI recommendations and action items.

I have proposed closure for these items, 1, 2, and 7. Is there a motion to accept the report?

DR. JADVAR: Is there a motion?

MR. GREEN: Second.

DR. JADVAR: Okay. All in favor, say aye.

(Chorus of aye.)

DR. JADVAR: Any opposed? Any abstention? Motion carries. Thank you. All right. I guess I can get started now. First of all, welcome. I want to thank Mr. Einberg and Mr. Williams for the comments and welcome to the ACMUI spring 2024 meeting.

I'm delighted to be the newly appointed chair of this distinguished committee and also continue working with a very knowledgeable and supportive NRC staff. I also want to welcome Dr. Joanna Fair as the new diagnostic radiologist on this panel. And with that, the next item on the agenda is Item No. 3, open forum. This is a forum where ACMUI will identify medical topics of interest for further discussions. Any items that the ACMUI members want to discuss at this session?

(No audible response.)

DR. JADVAR: Okay. Hearing none, we'll

move on to Item No. 4, medical related events. And this is done by Mr. Dimarco who will provide an update on the recent medical events.

MR. DIMARCO: Good morning, everyone. My name is Daniel Dimarco. I'm a health physicist here at the medical radiation safety team. And I'm here to give my update on the status of medial events for FY 23. Next slide, please.

So here we can see a chart of the medical events from the past five years, FY 18 to FY 23. Those numbers in the parenthesis in there, those are the total number of patients involved in each medical events if they are greater than the number of medical event reports. Just going through FY 23, we can see that the number of events generally coincides with how many events we've had the past couple of years, slightly less than some, slightly more in other categories, with a grand total 59 events this year which is about where the levels we see from the past few years. Next slide, please.

So, getting into the events themselves, we had one 35.200 medical event involving iodine-123. Next slide, please. This event was a wrong drug event where the patient was prescribed an Iodine-23 scan but instead received 162.8 megabecquerels of Iodine-

131 in a TBI scan. This scan was scheduled in the clinic's electronic medical system as a TBI scan with Thyrogen.

The patient was administered this first dose of Thyrogen. However, the technologist realized that the patient continued to have their thyroid before the second injection of Thyrogen. This patient was then administered the Iodine-131 injection, and the radiologist discovered the patient had been administered the wrong drug when reviewing the images post-injection.

And the RSO estimated the dose of the thyroid to be about 150. Next slide, please. The patient follow up reported no adverse effects. The root cause was determined to be human error.

The protocol to have all the patient records and lab work completed before the administration was not followed in this case. Additionally, the written directive did not specify any radioisotope, only that a total body iodine scan had been prescribed. The corrective actions included the creation of a new form requiring the inclusion of all relevant patient labs to be completed before signing the written directive. Next slide, please.

Coming into the 35.300 medical events, we

had 11 this year, 9 of which involve Lutetium-177 and 2 of which involved Iodine-131. Next slide, please. Our first event is a wrong drug event involving Lutetium-177 where one patient was prescribed a commercially available Lutetium-177 dotatate and another was prescribed a different dotatate under a new investigation drug label. The patient prescribed the commercially available Lutetium drug was instead administered the investigational drug.

This patient was given the correct activity, the correct chemical form. And through the correct route of administration, that root cause was determined to be human error. However, no adverse effects are expected. Additional notifications were made to the institutional review board considering that this involved an investigational drug product. Next slide please.

Our next event involved a patient overdose where a patient was prescribed 5.92 gigabecquerels of Lutetium-177 but it was instead administered 7.65 gigabecquerels. The RSO indicated that the technologist did not follow the written directive to verify activity before injection. A confounding factor for this is that a typical injection uses 7.4 gigabecquerels, but the

technologist did not recognize the updated dose from the position. And the corrective actions for this included updated procedures. Next slide, please.

This next event was a patient underdose where a patent was prescribed 7.4 gigabecquerels of Lutetium-177 but received at 70 to 75 of that dose. This was an administration using a syringe pump where 20 minutes into the injection, the patient reported a wet feeling on their hand where a leak was traced to the connection between the syringe pump and the patient's IV site. The bedding in the material had absorbed the majority if the lead and spill response protocols were initiated.

Estimates of material remaining in the vial, the contamination on the bedding, and patient dose rate measurements suggested an underdose of about 30 percent. That's where we got the estimated dose for that. The skin exposure was measured to be about under 10 centiSeiverts, and corrective actions included updated procedures and training, clarification that all future therapy administrations would be through secured connections. Next slide, please.

This next event involved a patient underdose of Lutetium-177 where the patient was

prescribed 7.4 gigabecquerels but administered only 5.83 gigabecquerels. During the administration, the technologists noticed drips coming from the tubing. An investigation after indicated that the patient had received 21.22 percent less dose than prescribed. The root cause was determined to be leaking tubing.

Additionally, the tubing from the same lot was also found to be leaking in a post-treatment investigation of the rest of the equipment the clinic used. Corrective actions including removing that specific lot from use and notifying the vendor of the defect. And additionally, the licensee updated procedures to visibly check for leaks before administrations. Next slide, please.

This next event was another Lutetium-177 patent underdose where the patient was prescribed 7.4 gigabecquerels but received 4.48 gigabecquerels. In this administration, they were specifically using Pluvicto. But the normal apparatus use for administering this drug was not available due to supply chain issues.

Instead, they used a similar pressurized apparatus for injection. A leak was identified at the rubber septum of a vial in a shielded storage container. And the root cause was determined a

pressurization of the vial. Typically, the manufacturer does not recommend pressurizing the vial. And so, another dose of Pluvicto was administered to replace the underdose administration and was administered without incident. Next slide, please.

Similar to the previous event, this was another patient underdose where a patient was prescribed 7.4 gigabecquerels and received 4.77 gigabecquerels. As before, the normal administrating apparatus for administering Pluvicto was not available. They used a pressurized apparatus, similar root cause, similar leak from the shielded storage container. However, in this one, the patient was monitored during the rest of the treatment regime and the appropriate equipment will be used for following treatments. Next slide, please.

This event involved a wrong drug for Lutetium-177 where we had two separate patients, one prescribed 7.4 gigabecquerels of Lutetium-177 dotatate, another prescribed 7.4 gigabecquerels of Lutetium -- I can't --l the other one, textraxetan, yes. These vials were switched, and each patient was administered the incorrect drug. The root cause was determined to be complacency and lack of training.

Additionally, both doses were identical looking, and the shipping containers were similarly colored. Corrective actions including implementing a new scheduled process, so Lutathera and Pluvicto treatments are not scheduled on the same day and the institution of a dual verification process. Additionally, the licensee provided re-education on package checks and patient verification. Next slide, please.

This event was a patient underdose involving Lutetium-177 where the patient was prescribed 7.4 gigabecquerels but received 3.92 gigabecquerels. The injection occurred without incident. However, post-treatment investigation discovered residual radiopharmaceutical in the injection tubing which gave an estimate of the underdose. The root cause was determined to be human error, and the corrective actions included increasing the mandatory saline flush from 25 milliliters to 250 milliliters, additional staff training, and strict vetting of technologists for therapy administrations. Next slide, please.

This next event was also a patient underdose involving Lutetium-117 where the patient was prescribed 7.4 gigabecquerels but received only

5.11 gigabecquerels. Again, the injection occurred without incident. The post-treatment investigation discovered residual radiopharmaceutical in the injection tubing. And the root cause was determined to be human error with additional corrective actions, including an increase of the mandatory saline flush, staff training, and strict vetting of technologists for therapy administrations. This isn't a repeat event. This is two events from the same clinic, I believe. Next slide, please.

This next event was a patient overdose involving Iodine-131 where the patient was prescribed 2.78 gigabecquerels but was administered 3.7. Two doses of Iodine-131 were prepared for two separate patients. However, when preparing the dose for the first patient, the technologist mistakenly assayed the second dose. And so the first patient was inadvertently administered intended for the second patient.

This mistake was discovered prior to treating the second patient. The root cause was determined to be human error. And the corrective actions included staff training on time-out procedures and a posting of a physical copy of these procedures on the wall in the therapy room. Next

slide, please.

This next event was also an Iodine-131 patient overdose where the patient was prescribed 740 megabecquerels but received 780 megabecquerels. The patient received the intended dose. However, the written directive incorrectly specified 20 microcuries instead of 20 millicuries.

No adverse effects are expected. And the corrective actions included combining the written directive checklist and the written directive prescription into one form. And the AU is also now required to circle the word millicurie or microcurie on the form, and the technologists have to sign off on the dose verification form on that.

There's an error on this. It should be that they received 780, 21.1 millicuries, not the microcuries. This is a written directive error event. Next slide, please.

Going into the 35.400 medical events, we have three, one involving an eye plaque and two involving Cesium-131 brachytherapy. Next slide, please. This first event, the Iodine-125 eye plaque where the patient was prescribed 8,500 centigray but received 5,700 centigray. The licensee believe that the eye plaque may have shifted over the seven-day

treatment. However, an update is still pending for this event. This is all the information I have for this event. Next slide, please.

This next event is involving Cesium-131 with a patient underdose where the patient was prescribed 11,500 centigray but received 5,570 centigray. They had planned -- the licensee had planned to implant a total of 98 seeds with a total of 10.46 gigabecquerels. However, after the treatment, they noticed that 37 seeds were unused and only 70 total were implanted. The root cause of this was determined to be swelling and excessive bleeding during the treatment which caused coagulated blood in the Mick applicator for these seeds. And corrective actions included revision of the procedures. Next slide, please.

This slide was also a patient underdose of Cesium-131 where the patient was prescribed 6,000 centigray but only received 3,700. The patient was implanted with seeds totaling 1.42 gigabecquerels. However, following implantation, the patient was diagnosed with a medical condition that necessitated the immediate removal of the seeds.

All the seeds were accounted for. The dose was calculated. And this incident was

discovered during a routine safety inspection. No corrective actions were taken. Next slide, please.

These next medical events are the 35.600 medical events of which there were eight. Next slide, please. This event was a wrong site event which involved a 185 gigabecquerel Iodine -- or Iridium-192 HDR unit where the cylinder had inadvertently shifted during a vaginal treatment by 3.5 centimeters. However, for this event, the update is still pending. Next slide, please.

This event was another wrong site involving 192.4 gigabecquerel Iridium-192 HDR unit. The patient was prescribed 1,800 centigray in three fractions. All of the pre-treatment verifications, the CT planning, the plan review, the time-out, and the device insertion were all completed without incident.

However, during the first fraction, the patient notified the AU that the cylinder was in the wrong place. This administration was stopped 111 seconds into the treatment. And it was discovered that the cylinder had been placed into the patient's rectum instead of the vagina. Next slide, please.

After removal of device and discussion with the team, the treatment resumed with the correct

placement of the device. The remaining fractions were adjusted for this error and the dose to the rectum was estimated to be about 239 centigray. No adverse effects are expected, and corrective actions included additional training, including verification that the device is in the correct anatomy. Next slide, please.

This event was a patient overdose where a patient was prescribed 500 centigray in three fractions for a total of 1,500 centigray to the keloid skin surface. However, this patient was mistakenly administered the fully 1,500 centigray in one fraction. The medical physicist started the treatment plan based on the AU intention.

However, that original medical physicist was called away to another treatment and a second medical physicist finished that treatment plan. The second MP set the prescription to 15 Gray, not realizing this was a total dose, not a fractionation dose. And this mistake was caught during the post-treatment bookkeeping. Next slide, please.

No adverse effects are expected. The root cause was determined to be human error. And the corrective actions included specifying that a single MP be present throughout the whole planning and

treatment process, the implementation of a formal handoff process, more descriptive process checks, and a mandated pre-treatment time-out. Next slide, please.

This event was a patient underdose where a patient was prescribed four treatments of 500 centigray but received 156 centigray on the fourth treatment. The HDR unit have an error during this treatment indicating a source retraction issue. The right and left partial ring treatments were administered but not the tandem.

The root cause was determined to be a failure of the HDR motors. Additionally, the licensee had to use an applicator that was not for use -- that was not approved for use with the Flexitron system, which resulted in the source capsule becoming stuck during treatment. The correctives including equipment testing, a hold on the program root cause analysis, evaluation of policies and procedures, and additional training. Next slide, please.

This event was another patient underdose involving a 251.6 gigabecquerel Iridium-192 HDR unit. The patient was prescribed five fractions of 600 centigray but received less than 50 percent of the

fraction for the first two. The planning had mapped channels to specific catheters.

But post-treatment review discovered that during the administration, the channels had been incorrectly mapped. The adjustments were made in the following fractions to ensure appropriate tumor coverage and tissue sparing. So, no adverse effects are expected. And corrective action included updated procedures and checklists. Next slide, please.

This next event was another patient underdose involving a 275.28 gigabecquerel HDR unit. The patient was prescribed 1,350 centigray but administered 326.56 centigray. During treatment, the AU observed that the transfer stretcher was pitched toward the patient's head and interrupted the treatment when they noticed that. Fifteen of the 17 needles had been extracted approximately 2 centimeters during the treatment time. Patient was monitored for any adverse effects after this event, but none were expected. Next slide, please.

The root cause was determined to be an issue with the hydraulics and the transfer stretcher with a lack of attention to the patient as a contributing factor. Corrective actions including amending procedures to maximally lower the stretcher

during treatment. And the state during their review also recommended evaluating the roles of individuals present during treatment to ensure continuous patient monitoring. Next slide, please.

This next event was another patient underdose involving a 329.3 gigabecquerel Iridium-192 HDR unit. The patient was prescribed 750 centigray per fraction, but was administered 12.7 centigray in the third fraction. During this treatment, the HDR unit was unable to detect on the transfer tubes connecting it to the application, which resulted in this partial delivery of the fraction. When the licensee called the field service engineer, they determined that the HDR unit selector should be recalibrated after which the unit functioned correctly. And then the patient was successfully treated the following day. Next slide, please.

This next event was a patient overdoes involving a 327.5 gigabecquerel Iridium-192 HDR unit. The patient was prescribed five fractions of 600 centigray but received a full 3,000 centigray in a single fraction. During the treatment, the MP misread the written directive and delivered the full 3,000 centigray in a single fraction. The patient

was administered -- was monitored following this treatment. And no adverse effects were observed. Next slide, please.

The root cause was determined to be human error, specifically the licensee using two treatment planning systems and the MP reading the secondary plan instead of the primary plan where the secondary plan noticed only the full treatment dose. The corrective actions included having one person perform the planning and another person performing the verification with each signing off before treatment. Additionally, a generic table of expected treatment times based on dose was developed to be used. And then post this event, the state reported that the corrective actions taken were suitable. Next slide, please.

Getting into the 35.1000 medical events of which we had 36 this year, one involving seed localization, one involving intravascular brachytherapy, one involving gamma stereotactic radiosurgery unit, and 33 involving Y-90 microspheres. Next slide, please. This first event was a failure to explant for radioactive seed localization. A patient went into surgery to have all these localization seeds explanted the day after

they had been implanted.

Ten months later, however, discovered that the seed remained in the patient. The previous surgery had removed just a surgical clip instead of the seed. The calculated dose to the tissue was 74 centigray. And the seed will be removed in a future planned surgery. Next slide, please.

This next event involved a wrong site with the intravascular brachytherapy. Excuse me. The patient was prescribed 2,300 centigray which was delivered to the wrong treatment site. This involved a 3.62 gigabecquerel Strontium-90 source.

During treatment, the cardiologist used fluoroscopy to determine the treatment site. And post-treatment review of the images could not accurately assess the location of the source. But afterwards, the primary -- the prescribing physician determined that the dose had been delivered to another part of the vasculature proximal to the intended location. Next slide, please.

No permanent damage is expected. However, the root cause was determined to be human error. The cardiologist misread the images due to a poor quality of these images and obscuration of the images by additional medical equipment. Corrective

actions included additional training, procedure modifications, and an agreement for an independent assessment of a dose by a medial physics consultant. Next slide, please.

This next event was a patient underdose involving a Gamma Knife. The patient was prescribed 1,500 centigray but was only delivered 44.11 centigray. For this treatment, they had planned 13 shots, but the unit malfunctioned after completing only 3.

The error could not be resolved by the licensee and required a call-out to the service technician. This technician identified and repaired a worn sector drive assembly. And the patient was rescheduled for successful treatment. Next slide, please.

Getting into the Y-90 events, we're going to start with all the TheraSphere events and then go into the SIR-Sphere events. So, this one was an underdose for a TheraSphere event where the patient was prescribed 1,500 centigray but received 79 -- or 15,000 centigray but received 7.905 centigray. The root cause was determined to be a significant back pressure with overflow of saline into the pop-off vial.

This back pressure was significant enough to prevent delivery of the full dose. No adverse effects are expected. And corrective actions including a monitoring of the pop-off vial during administration for back pressure in addition to the normal checks. Next slide, please.

This was a Y-90 underdose where the patient was prescribed 2.11 gigabecquerels but received 0.927 gigabecquerels. Unfortunately, the investigation is still ongoing. So, this is all the information I have to give today. Next slide, please.

Next event was another underdose where the patient was prescribed 1.7 gigabecquerels but administered 1.3. The administration occurred without incident or was seen to occur without incident. And the underdose was determined to be clinically effective. However, post-treatment calculations revealed this underdose of which the imaging of the waste determined the majority of the remaining dose remained in the vial. Inspectors concluded that the practitioner did not tap the vial sharp enough against a hard surface prior to administration, otherwise known as inadequate agitation of the vial. And corrective actions included checklist revision to better describe does

vial preparation and additional training in these revisions. Next slide, please.

This next underdose was a patient prescribing 40,700 centigray but receiving 31,320. The AU discovered that a significant amount of residual dose was in the vial post-treatment. The delivery kit was returned to the manufacturer where a kink was discovered in the microcatheter by the manufacturer.

Additionally, there was evidence of low flow of microspheres during delivery. No adverse effects are expected. The dose received was determined to be therapeutic, and corrective actions included observation of the next case by the lead IR physician involving this specific AU for this event to ensure correct administration. Next slide, please.

This next event was an underdose where the patient was prescribed 6.7 gigabecquerels but received only 5.02 gigabecquerels. The root cause was determined to be air in the tubing during administration. And no adverse impacts of the patient are expected, and the dose was determined to be medically significant. Next slide, please.

This next event was another underdose

where the patient was prescribed 1.24 gigabecquerels, received 0.715 gigabecquerels. During the treatment, the physician noted that the microspheres required higher pressure to deliver, and the spillover vial had a high volume of microspheres. Post-treatment surveys confirm this large portion of microspheres had not been delivered.

Root cause was suspected to be failure of the needle or the equipment since no other operating steps showed signs of failure. The patient was scheduled for a follow-up treatment. And the equipment will be returned to the manufacturer for investigation when sufficient decayed. Next slide, please.

This next event was another underdose where the patient was prescribed 17,500 centigray but received 3,170 centigray. The physician noted resistance during administration and the pressure vial was noticed to be filling with saline. The treatment was stopped, and a plug of microspheres was discovered in the line.

This plug was dislodged, and saline was flushed eight times. But ultimately, the procedure was terminated since it was clear the administration was not successful. A follow-up procedure was

scheduled. And the treating equipment was returned to the manufacturer for investigation. Next slide, please.

This event involved a wrong site where the patient was prescribed 3.07 gigabecquerels to the right lobe of the liver but received this dose to the left lobe. The Tech-99 planning study indicated primary deposition in the right lobe with small deposition in the left lob. However, the primary distribution was actually to the right lobe of the liver. The treatment had been planned to the right lobe under a different written directive, so -- the treatment had been planned to the left lobe of the liver under a different written directive. So, no adverse effects to the patient are expected. Next slide, please.

Corrective actions included a new process where nuclear medicine contacts interventional radiology when images indicate any activity in an unintended area. Additionally, all AUs have been directed to consider all distribution pathways discovered during the planning study and follow-up treatments. And the state inspectors determined that all procedures were followed, and corrective actions implemented were acceptable. Next slide, please.

This was another wrong site where the patient was prescribed 1.41 gigabecquerels but received 63 grays. Post-treatment imaging determined that some activity was taken up by unintended segments of a liver. The procedure was determined to be performed correctly, but the activity was transferred due to complex hepatic flow.

No adverse effects are expected. And the licensee indicated that the procedure was performed successfully and that this is an expected risk of the procedure. Therefore, no corrective actions can be taken. This even is still currently under review. Next slide, please.

This event was a Y-90 underdose where the patient was prescribed 0.98 gigabecquerels but received 0.77 gigabecquerels. The treatment was performed without incident. However, post-treatment surveys discovered a significant number of microspheres remaining in the source vial.

The dose administered was determined to be clinically sufficient. The root cause was unable to be determined. And the licensee plans to return the device to the manufacturer for examination after decay. Next slide.

This was another Y-90 underdose where the

patient was prescribed 1.08 gigabecquerels but received 0.784 gigabecquerels. The treatment occurred without incident. But post-treatment surveys reveal microspheres in the waste vial.

Imaging revealed that the microspheres were stuck at the juncture of the outflow tube and the microcatheter. No adverse effects are expected. And a reactive inspection did not identify a clear cause.

The increase in pressure might have been caused by tortuous anatomy or other microcatheter issues. The procedure was followed correctly, and no problems were indicated during the administration. So, the licensee plans to return the device to the manufacturer for investigation. Next slide, please.

This event was another underdose where the patient was prescribed 12,000 centigray but received 9,140 centigray. No indication that anything was wrong during the administration. And the physician had indicated that four saline flushes went into the patient with no problem.

The treatment was observed by the RSO as well as a manufacturer representative. And they indicated that all procedures were followed. Post-treatment, microspheres were discovered attached to

the bottom portion of the septum and clumped in the microcatheter that did not cause clogging. The licensee plans to send this device to the manufacturer for investigation following decay. Next slide, please.

This was another Y-90 underdose where the patient was prescribed 539.46 megabecquerels but received 36.74 megabecquerels. The physician stated that the procedure proceeded normally aside from slightly more resistance. However, subsequent imaging showed little to no activity in the patient, and surveys of the waste revealed that the majority of the activity remained in the tubing. For this administration, they used a specialized catheter for Y-90 administrations, specifically the TriNav 130 centimeter was used with a 20 centimeter extension catheter. Next slide, please.

The root cause was determined to be the use of this extension catheter. The larger internal diameter of the extension reduced the saline velocity, which caused the microspheres to fall out of suspension. This patient underwent a repeat procedure with no issue. And corrective actions included training, no longer using extension tubing, and ordering larger catheters for use -- or longer

catheters for use. Next slide, please.

Another underdose, this patient was prescribed 753 megabecquerels but received 215 megabecquerels. Measurement of a vial following treatment showed a significant amount of activity remaining. And the root cause was still under investigation but is suspected to be due to a kink in the catheter. The patient will likely require further treatment. And the licensee will send the device back to the manufacturer for investigation following decay. Next slide, please.

This next event was a Y-90 underdose where the patient was prescribed 2.54 gigabecquerels but received 0.13 gigabecquerels. Post-treatment surveys discovered microspheres blocked in a tubing connector. But no spillage or contamination was identified. And the investigation of this event is still ongoing. Next slide, please.

This was another Y-90 underdose where the patient was prescribed 518 megabecquerels but received 31.45 megabecquerels. An obstruction was noticed nearly during the treatment. And so, the administration was halted following this discovery. Excuse me.

A similar event has occurred at this

licensee regarding the Y-90 devices from the same batch. And so, all microsphere administrations from that batch have been paused. And the investigation for this is still ongoing. Next slide, please.

And so, this was another event from that same batch where the patient was prescribed 742.22 megabecquerels but received only 34.41 megabecquerels. Same as before, the obstruction was noted early during the treatment. And the Y-90 devices from this batch have been paused. All administration from this batch have been paused. Next slide, please.

This next event is another Y-90 underdose where the patient was prescribed 1.03 gigabecquerels but received 0.64. During the treatment, a 2.4 French TriNav anti-reflux catheter was attached to the delivery device. And so, no microspheres were found in the tubing or delivery system post-treatment. However, surveys of catheters found high residual activity remaining. And post-treatment scans revealed activity in the left hepatic lobe with unusual uptake in the spleen/gastric region. Next slide, please.

The root cause is suspected to be a microcatheter rupture during administration,

resulting in high activity in the catheter and unusual distribution. The patient was admitted for observation and remained asymptomatic. And corrective action included discontinuing the use of this anti-reflux catheter and retraining on Y-90 administrations. Next slide, please.

This next event was another underdose where the patient was prescribed 1.282 gigabecquerels but received 0.981. The post-treatment imaging revealed microspheres remaining in the tubing and the root cause determined to be human error. Specifically, the AU could not recall if the microcatheter connection had been placed in the holder on the extension arm.

Additionally, the dosimeter did not detect any microspheres moving through the tubing during administration. No adverse effects are expected. And the corrective actions included reminders of best practices during a Y-90 treatment and additional surveys of the tubing for verifications that microspheres have moved through during the treatment. Next slide, please.

This next event involved a wrong site error where the patient was prescribed 0.8 gigabecquerels for one liver segment and 1.93

gigabecquerels for another where these doses were mistakenly switched during administration. During the administration, the physician asked for the first dose but was brought the second. After verbally reading the dose, this vial was connected and delivered. The root cause was determined to be human error. And the corrective actions included a radiation dosing education program with event background and call back procedures as well as additional training for personnel. Next slide, please.

The next event was a Y-90 underdose where the patient was prescribed 1.377 gigabecquerels but received only 0.451 gigabecquerels. The treatment was administered according to manufacturer requirements with no errors. However, during the second saline flush, a technologist noticed that the liquid was pooling inside the acrylic pot within the led pig.

Multiple attempts to stop this were unsuccessful and the administration was halted. Next slide. Surveying the waste container gave an estimate of the activity that was administered. And the patient will be evaluated at follow up for future treatment.

No root cause was able to be identified. No specific corrective actions were implemented due to this. And the administration kit will be returned to the manufacturer for analysis after decay. Next slide, please.

This event was a Y-90 wrong site event where a patient was prescribed 666 megabecquerels to segment 5 of the liver but will receive 520 to segments 7 and 8. A stenosis in the target vessel required changing the treatment vessel to the origin of the vessel rather than further down. And so, an unexpectedly large volume of the microsphere refluxed into wrong segments of the liver. No corrective actions were taken. Next slide, please.

This event involved the Y-90 underdose where the patient was prescribed 1.377 gigabecquerels but received on 0.903 gigabecquerels. During the administration, the licensee suspected low flow rates had caused occlusion in the catheter. And after analysis by the manufacturer, they had determined that the injector needles had been bent at a 90-degree angle and there was a kink in the tubing at the pinch clamp.

However, they could not verify if these were problems pre- or post-treatment. Blood clots

and microspheres were also found in the waste collection vial. Next slide, please. The root cause was determined to be a low flow rate, the cause of which could not be identified. No adverse effects are expected, and the dose was determined to be medically sufficient. Corrective actions included the use of an electronic dosimeter near the patient to identify blockages or buildup of material between the device and the patient. Next slide, please.

This event was a Y-90 wrong site error where the patient was prescribed 848.4 megabecquerels to the left lob segments 5 and 8 but received 847.3 megabecquerels to left lobe segment 4. Specifically, this was a written directive error. The dose was intended to be given to segment 4, but a typographical error resulted in the wrong written directive being produced.

No adverse effects are expected to the patient. And corrective actions included specifying the treated segment in writing with a formal review of the directive by the treating IR. Additionally, the treatment quality control will include a verbal verification of the treatment site prior to administering the dose. Next slide, please.

Going into the Y-90 SIR-Spheres events,

this was an underdose where the patient was prescribed 536.5 megabecquerels, 802.9 megabecquerels, but received 196.1 megabecquerels and 455.47 megabecquerels respectively. This patient had two vials of microspheres for this treatment. However, the manufacturer could not find any residual microspheres in the device and testing received no errors.

This was post-treatment the device had been given back to the manufacturer for analysis. The root cause was determined to be a leak between the delivery system and the administration catheter. And corrective actions included procedure modifications, additional training, and obtaining new equipment. Next slide, please.

This event was a Y-90 overdose where a patient was prescribed 1.6 gigabecquerels and 0.7 gigabecquerels but instead received 2.34 gigabecquerels and 0.77 gigabecquerels respectively. This was a single written directive for a split dose administration, two doses for two separate locations. However, the RSO inadvertently entered the total of both doses into the prescribed dose section of the treatment planning spreadsheet.

Additionally in this spreadsheet, they

only used gigabecquerels as a unit which disguised the unexpectedly large dose for the first administration. No adverse effects are expected. And corrective actions included revision of procedures and the calculation spreadsheet, preparation of separate written directives for split doses, listing the activity in both gigabecquerels and millicuries on relevant forms and containers, and creating a no distraction zone in the preparation hot lab. Next slide, please.

This event was a Y-90 underdose where the patient was prescribed 0.407 gigabecquerels but received 1.4 gigabecquerels. This was intended to be a two-step successive administration where the technologist drew 2.23 gigabecquerels for the first step instead of the intended 0.223 gigabecquerels. My mistake. This is should be an overdose, not an underdose.

Statis administration of this dose was estimated and no further administration to the patient occurred. Next slide, please. The root cause was determined to be a lack of standardized written nuclear medicine procedures for microsphere administration verification and inexperience by the administering technologist. The corrective actions

included formalized staff retraining, rewritten procedures, establishment of a secondary verification during dose preparation, the use of a volume determination spreadsheet, and the use of a chart of expected measurements for known amounts of activity. Next slide, please.

This was a Y-90 wrong site event where the patient was prescribed 1.32 gigabecquerels to the right lobe of the liver but received 1.35 to the left lobe of the liver. The root cause was determined to be human error. And no adverse effects are expected.

The left lobe of the liver was intended to be treated under a different written directive after this event occurred. And that written directive intended to have a dose within 20 percent of this administered dose. The corrective actions included procedure modifications and additional training. Specifically, the procedure was updated to require verbal verification of a lob being treated and an additional review by the physician prior to treatment. Next slide, please.

This next event was a Y-90 underdose where the patient was prescribed 53.65 megabecquerels but received 19.61. The root cause was determined to be very small amount of dose attempted to be drawn

up. Specifically, they noted it was 0.07 CCs of volume.

Multiple attempts to draw this dose caused the dose vial to not have a complete seal. And so, the AU had decided to stop the procedure. And no adverse effects are expected. Next slide, please.

This was another Y-90 underdose where the patient was prescribed 700.41 megabecquerels but received 557.59 megabecquerels. The treatment was delivered without error. However, further investigation discovered that this procedure had reached stasis. The root cause was determined to be failure to identify statis and lack of sufficient training. Corrective actions included additional training. Next slide, please.

This next event involved a Y-20 underdose where the patient was prescribed 3.39 gigabecquerels but received only 2.02. This did not appear to involve statis. And root cause was determined to be equipment failure. And the corrective actions included disposal of the involved equipment. Next slide, please.

Another Y-90 underdose. The patient was prescribe 495.8 megabecquerels but received only

305.62. The procedure occurred without incident, nothing that there was no statis involved. However, post-treatment survey of the tubing found a significant amount of microspheres remaining in the catheter.

No leakage or contamination. Excuse me. The procedure was followed correctly, and the equipment used was in line with manufacturer recommendations. And so, the root cause was suspected by the manufacturer to be a premature air pause. And corrective actions included refresher training. Next slide, please.

Another Y-90 underdose where the patient was prescribed 399.6 megabecquerels but received 160.2. They noted an appropriately sized catheter was used. And vascular access to the treatment site was unusually tortuous.

The manufacturer representatives observing the treatment noted no deviations from recommended protocols. And the root cause was suspected to be a collection of microspheres on the catheter walls due to tortuous anatomy or excessive bends in the line. Correction actions for this event are pending. Next slide, please.

Okay. So that was all of the events for

this fiscal year of 2023. And so, I'll just get into a bit of a summary for some of these collections. So, starting off with the 35.300 events, these were primarily Lutetium-177 human error underdoses.

Some of the major ones that I've seen this year were a mix-up of Lutathera and Pluvicto which we've talked about before as well as mix-ups on the patients themselves as well as supply chain issues for delivery equipment. I don't have my finger on the pulse on that. So, I don't know if those issues are resolved yet.

But I know that those supply chain issues can definitely attribute themselves to some of these events this year. But we will be having an information notice on 35.300 events coming out very soon, I believe. Next slide, please. Going into the 35.600 events, these again were primarily human error events.

But there were a few equipment failures this year. There were multiple events this year where they had full dose delivery in on fraction instead of the fractionated doses. A lot of those, you can see were exacerbated by teams not focusing, teams handing off responsibilities to other members of the team.

So hopefully, this will help keep people

on their toes when they review these events. We also had a couple here same as last year with incorrect anatomical placement for these events. Next slide, please. Going into the 35.1000 events, I'll focus just primarily on the Y-90 microspheres ones.

As we've seen in years before, these are primarily TheraSphere events and they're primarily underdoses. One thing that I saw this year a lot in these events which I'm sure that they've done it before. But there was a lot of collaboration with the manufacturers this year sending these devices back for analysis, specifically calling it out in the events that representatives were there to look after a lot of these treatments which I think is a great thing.

I'm sure they've done it before. They just haven't told us. But I've noticed it in the event reports this year a lot. And one thing that I also saw this year were possible complications with catheter supplements, not the catheters themselves but things like extensions and anti-reflex cages and other things like that.

And so those might be exacerbating the events themselves for this. And I think that's everything. Next slide. Yes, my acronyms. Next

slide. You can just go to the end. Next slide. Any questions?

DR. JADVAR: Thank you, Mr. Dimarco, for that very comprehensive report. Do we have any comments or questions from the ACMUI members? Dr. Angle?

DR. ANGLE: Yeah, John Angle reporting here. I know we've talked about this before. But the underdosing Y-90s are unfortunate but not a serious clinical event. I just wonder if we should reconsider these being medical event reporting to this committee or at least how we present them.

DR. JADVAR: Any thoughts on that comment? Dr. Harvey?

DR. HARVEY: I think by the definition and by the law, I mean, they have to be reported as medical events because they are below and they're outside the tolerance. But I certainly understand what you're bringing up, Dr. Angle.

DR. ANGLE: A follow-up question to that is that the legal requirement is just to report the dose was not delivered. But the clinical scenario and the clinical investigation we do on those perhaps is not required. Is that a true statement? You're putting a lot of energy into looking into the clinical

situation with all of these and not necessarily leading to any change. I just want to make sure that's worth our investment of time and energy.

MR. GREEN: Dr. Angle, this is Richard Green. I think I heard what you're saying. We had a very descriptive of each event. And it might be better -- they are reportable. They are in the regulations.

But I wonder if just a summary of the collection of events rather than each of the 38 -- I don't remember the number -- of each event of what happened. There's really not much that this committee could do with that clinical information of each patient's case. Is that what you were thinking about?

DR. ANGLE: Yes, I think that would be, I think, efficient.

DR. HARVEY: I think that the underdosing is still a very important consideration. The objective here is obviously to get the proper amount of activity to the patient. So, I think an analysis of these underdoses is important and looking for any trends or any problems or anything that could be helpful for other licensees to help prevent those underdosing so we get the correct amount of activity

in the patients. I do recognize the burden aspect that you gentleman are talking about. Thank you.

DR. ANGLE: I would like to ask one additional question. Would it be possible in these presentations to use one of the available Harm Scores and perhaps also a categorization of the etiology were we could look at trends in the etiology over a course of years, in other words, device failure or human error? And I know we do this.

But there are published, I think, guidelines for these things. I wonder if part of this presentation we could have a Harm Score, a categorization of cause, and then perhaps even some score of preventability because I think to your point, Richard, if we're going to look at this, I feel like we're seeing the same thing over and over again. Nothing changes. And I feel some obligation that we need to either step back or step forward on this and not remain neutral on this.

MR. DIMARCO: Daniel Dimarco. So, I will answer those questions by going back to your first statement with some of the things you said, you asked for before. In 35.3045, the event reporting requirements, there are specific requirements for the information that is reported. And one of those

requirements is things like corrective actions, adverse effects to the patient, things like that.

And that's for all events, including the Y-90 underdoses. So, we always get that information at least when we don't have updates pending for that. As for your second cause for that, I would say that going back to that 3045, we have very specific requirements for what to report for medical events. And as you see, they don't always give us anything more than the bare minimum of information for some of these events.

We specifically can't go out and ask for some of that information for things like preventability and Harm Scores and things like that. I would say for looking at those trends over more years, maybe the medical events subcommittee could take that on since they already look at these events for a longer spread of years than I do in my annual presentation. That's something that I could bring up to that subcommittee. And maybe with their more clinical knowledge, more on the ground knowledge, be able to give you better insights than I could.

MR. OUHIB: This is Zoubir, if I may. Can you hear me? Yeah, I'm a little bit sort of perturbed about the answer of a human error which is

a very generic statement in reporting an event. And I think we need to hear more from the users about what exactly was that human error.

Give us some very specifics. And that's not for sort of punishment or anything like that. But that's more for other users to learn and understand if you do something like this or if you don't do something like this, here's the outcome.

And I think we need to sort of try to get a little bit more information instead of just saying this was a human error basically. And then certainly when the user investigates this furthermore to provide that, and it would be beneficial to other users that to avoid that. The other item that is that I've seen a lot of devices being sent back to the manufacturer for evaluation and all that.

And I guess my question is that what is this going to provide to the community? Or is that information going to be between that particular user and the manufacturer? And the rest of the users will never know that, oops, this is what could happen. This is what actually happened and avoid doing this and so on and so forth. That's all I have.

DR. JADVAR: Thank you. Just I want to echo what you just said, Zoubir, because I had exactly

the same, I was going to ask about this. It seemed to me that there's a trend of these manufacturer problems and it seems to be systematic.

And I was wondering, are there specific manufacturers? What are these problems and how are they popularized to the general public of what these problems are and why they are not solved if it turns out to be manufacturing problem? But Zoubir, I think, beat me to that. Please, Mr. Green.

MR. GREEN: Mr. Dimarco, on page 34, you very nicely gave us a listing of all 33 medical events that involved spheres and broken them down this many TheraSpheres, this SIR-Spheres, and this many that are unknown. And on page 80, you also did a similar thing where you said this many were wrong site, this many were overdoses, this many were underdosed. I think it'd be very effective if you were to do a similar process to say of all these Y-90 administrations, these are the presumed causes and these are the implemented correct actions.

We could see a summary because you've got 33 here. And you went through all of them very detailed. But in my mind, I can't put together. So, what's the common theme? Okay?

You've done that with -- at the start,

there's this many of this kind. And at the back end, you say, this many were too much and this many were too little. But if you could make an attempt to say summarize the -- what are the -- again, human error doesn't tell us much as Mr. Zoubir has said.

But if they can say, I failed to rise adequately or I kinked the needle. Those are human errors. But at least we know something about it. Thank you.

DR. JADVAR: Any other comments from the ACMUI -- oh, sorry. Josh, please.

MR. MAILMAN: I have several. We've talked about this at the last meeting. These numbers in isolation are interesting but don't give us an idea of the general trend. Are the medical events going down per the number of procedures being done?

It's really hard to tell if we're getting better or if we're staying the same or if we're getting worse. So again, not on you. It's more of knowing what the total number is that we're looking at and are we getting better at reducing errors?

I know we'd like an absolute zero. But as some of these new therapies come online, I'm thinking of PSMA treatments. We're going to see a hockey stick number of treatments.

If we end up relatively flat on new medical errors, with that, I think we're doing a much better job. While I'd like to get to zero again, it would be good to know what the denominator is. So that's an overall thing.

One, and I didn't write the whole number down. It was in the Lu-177 ending with 531. One of the corrective actions, which I've heard from other sites as well, is to perform the total 177 treatments and the PSMA treatments on different dates. I don't understand how that's a sustainable corrective action.

There are going to be days in every clinic where you're going to need to dose someone who needs it. And I think this is a kick the can down the road solution. That is not scalable and teachable I think is the right word that I'm looking for here.

It really is an unteachable event to say this is going to apply to everywhere, maybe a small center. But past that, I don't see how that's a workable solution. I have two more points.

We've gotten into this conversation before on Lu-177 as opposed to Y-90 administration. Lu-177 is obviously put in by corridor by other methodologies. And we talk about administrative dose

all the time. It would be good to know not only what they received as the administrative dose versus what they were prescribed.

But if there could be a footnote to say what would be the absorbed dose because we know not all of the administrative dose hits target, most of it up to 50 percent. At least in header 1 and header 2 was created by the kidney. So, if we're slightly underdosing but yet we're just losing a little on the kidney, it would be good to know that the patient is really receiving a therapeutic dose.

Back to Dr. Angle's question about what really is going on and whether it's been an effective dose or not and whether the patient is getting the efficacy they -- and I don't know if you can add that to a form or not. But it would be an interesting sideline. And lastly, the one thing that hits me throughout this presentation is that -- and it may already be done and there may be an SOP for this all over the place.

But if someone is under any of these one, 300, two -- I'm not sure the total number we just went through. But how are patients informed about this and what corrective actions were there? Are they told and are they led to understand what the

implications are and how to follow up? Those are my questions or comments.

DR. JADVAR: Thank you, Josh, for those comments. I think Dr. Katie --

DR. TAPP: Yes, this is Katie Tapp. Going back through those, the first one about getting the denominator for the events, for the Yttrium-90 microsphere brachytherapy, both the manufacturers today did send us their vial shipped out. We've had that data in the past, and we have done a quick analysis.

But she's done analysis to confirm that the number of events divided by the number of vials shipped which is what they're available to give us has stayed relatively flat over the years. So, there is not an increasing trend. This is a -- it's trending -- it is staying relatively flat if not going down slightly.

I'm looking at Sarah Spence because she is the one who did that analysis and has done that. We cannot share that information because the number of vials shipped is proprietary. So, if we did that -- gave you that number here, we'd be sharing proprietary information.

Regarding the last statement about the

patients being told, it is a regulatory requirement that the authorized users notify the patients unless the authorized user or the referring physician believes that would be a detriment medically. I don't have the exact regulation in front of me. But there is a requirement that the patient is told about that. So, they're required to be told within 24 hours.

DR. HARVEY: Richard Harvey. Sorry to interrupt you, Dr. Tapp. I think your point is correct. The patients do have to be told within 24 hours. But oftentimes all the corrective actions, the root cause analysis haven't been completely performed. So, to Mr. Mailman's point, they may -- the patient may not understand or may not be told all of the corrective actions. But they certainly are notified of the occurrence.

MR. OUHIB: This is Zoubir Ouhib, if I may. I think to answer Mr. Mailman's question, I think Mr. Dimarco did show in one of the slides that they're having an increase on the 300, on the 1000. And overall, the total looked like a little bit up, per se.

I think the other item that we need to pay attention to, it's not the number but the implication of these case. In other words, were there

30 out of 50 that were significant or were there 2 out of 50 that were significant and impacted the patients? And I think that's very important.

DR. JADVAR: Mr. Green?

MR. GREEN: Dr. Tapp, it's great that you're getting the information from the Y-90 microsphere manufacturers. Has there been an arrangement established with the I-90 manufacturer when they come to market to get their information as well?

DR. TAPP: Not yet. But we can reach out to them when we get to that point.

MR. GREEN: That'd be great. Let's get a full deck.

DR. JADVAR: Dr. Harvey?

DR. HARVEY: Richard Harvey. I just want to address Josh's second point about the kicking the can down the road of trying to do Lutathera treatments and Pluvicto treatments on different days. I do agree that there can be sort of urgent studies or treatments that need to be done. And you might be performing some of these on these on the same day.

So, trying to put them on the same, they may be difficult. But most of these treatments aren't just in time. We need to do them tomorrow. So, we

do use this strategy where we schedule our Lutatheras and our Pluvictos on different days.

And I think it does help us to prevent medical events. So, I understand your point. I do think it can be a valuable strategy for some organizations.

DR. JADVAR: Josh, I think in one of your presentations in the past, I saw that you showed a picture of Lutathera patient doing a unit dose and the Pluvicto. They look the same. Is that correct? Has that been solved? But that has been corrected?

MR. MAILMAN: I believe it has been corrected or at least been made much clearer.

DR. JADVAR: Any other comments from the ACMUI members?

DR. ANGLE: Sorry, John. I'm going to ask one follow-up question to Mr. Mailman's comment. Why don't we make it our business to track how many doses are shipped in this country or how many doses are administered in this country?

I know you can't report it. It's proprietary information. But if it's worth our effort to follow the medical adverse events, I would think having this denominator would be essential part of the equation. I don't know.

DR. JADVAR: Good question. Dr. Harvey?

DR. HARVEY: Maybe -- this is Richard Harvey. Maybe Mr. Dimarco can maybe not report on the actual number. But maybe he can report on the trends in his reports if the NRC seems feet or if he thinks that's a good approach. Thank you.

MR. MAILMAN: Of course, that's incredibly hard to do with a single agent drug -- I mean, a single manufacturer drug because that would -- I mean, the challenge would be to amass that as we have more drugs in the same field that might become easier to amass that. Although some of them do release the number of doses they're doing publicly. But it may be worldwide versus U.S. Anyway, it's challenging. Just bringing it up to make sure we do what we can, meet the challenge.

DR. JADVAR: Great comments and a great presentation. I guess the theme is somewhat of a more digestible summary of what is going on so that we can have a better understanding of the trends and what needs to be done. But great report. I want to open it up to NRC staff. I know Dr. Tapp already discussed something. But anything else?

DR. VALENTIN-RODRIGUEZ: Yeah, let me look at my notes because I had a few things here that

I wanted to just address. So what Daniel was talking about what folks are reporting to us what information we're getting, and I'm going to talk about this, this afternoon. But Dr. Katie Tapp has the lead for developing a medical event, regulatory guide for all medical events.

And that's going to be issued as part of the proposed rule for extravasations which you all are reviewing right now. One of the things we did there was the best practices that you all recommended a few years ago about reporting medical events was incorporated into that guidance to provide licensees with examples as to what information is useful and what to report. But we're always open to your suggestions.

The one thing, Dr. Angle, regarding the Harm Scores, the categorizations we can definitely do. I mean, we have a plethora of information from years past. Score preventability, I think because we're not focused on practice of medicine and how effective of a dose is being administered but more rather as to ensure that the physician's directions or the written directive are followed. I don't think it'd be appropriate for us to do that type of trending. But we can certainly talk to the medical

events subcommittee and see if that's something that could be incorporated into their presentations. But as such, given our regulatory authority, it wouldn't be prudent for us to make points on that.

DR. JADVAR: Thank you, Dr. Valentin-Rodriguez. Any other comments from the NRC staff? I think we have -- okay.

MR. EINBERG: Yeah, Chris Einberg here. Yeah, I just wanted to say thank you for the great discussion and the feedback here. And Daniel, great presentation, very comprehensive.

And I know a lot of time and effort goes into putting that together. The feedback from what I heard was that let's try to relook at this presentation. We'll take that back. We'll try to bring it to a higher level, maybe summarize it somewhat so that there's more impactful discussions on this in the future. So, thank you for that discussion.

DR. JADVAR: Thank you very much. Well, we have time still. So, I want to open it up to any attendees in the room who wants to make a comment.

(No audible response.)

DR. JADVAR: Okay. And then perhaps we can go to any comments or questions from the remote

attendees. Celimar?

DR. VALENTIN-RODRIGUEZ: This is Celimar. For those who are in the virtual room, right now I'm having issues trying to unmute the entire room. So, for those who are on the phone, if you want to raise your hand, you will need to press star-5 and I will call on you and then enable your mic.

For those who are attending, just raise your hand and I will go ahead and enable your mic so you can comment. Again, if you're on the phone, star-5 to raise your hand. And if you're on the virtual room, just use the raise hand function at the top of your team's app or desktop app. And then I can enable the mic for public comment.

And as a reminder, please try to keep comments on the topic at hand which is medical events. Thank you. Dr. Jadvar, at this time, I don't see any hands raised.

DR. JADVAR: Okay. Well, thank you again, Mr. Dimarco --

(Simultaneous speaking.)

MR. OUHIB: If I may.

DR. JADVAR: Oh, sorry. Go ahead.

MR. OUHIB: This is Zoubir Ouhib. I just wanted to sort of let you know that the AAMP which is

the America Association of Medical Physicists has actually put together a task group report to deal with medical event reporting. In other words, the language, the information itself that is critical.

And that's actually going in print probably as we speak. I happen to be a member of that. Bruce Thomadsen who is a past member and chair of ACMUI was actually the chair of that report. And I think we're hoping that will help the medical physicist community to actually provide more information when it comes to a medical event.

DR. JADVAR: Thank you, Zoubir. Perhaps at some point you can give us a summary of what activities they are doing. Is that okay?

MR. OUHIB: I'd be happy to.

DR. JADVAR: Again, thank you. Again, Mr. Dimarco, thank you so much for your time and effort and energy on this very comprehensive report. With that, we move on to the next item, number 5. It's going to be. I was total it's Akesis Galaxy RTi unit committee report by Dr. Wolkov.

MR. EINBERG: Dr. Jadvar, we're considerably ahead of schedule right now. I wanted to propose that maybe we take a few minutes break since we don't have a break on the morning agenda

here. So, if that's acceptable to you.

DR. JADVAR: Absolutely, maybe 15 minutes until 10:30 Eastern Time.

MR. EINBERG: Thank you.

DR. JADVAR: Adjourned until 10:30 Eastern Time. Thank you.

(Whereupon the above-entitled matter went off the record at 10:18 a.m. and resumed at 10:32 a.m.)

DR. WOLKOV: To a critically located small intercranial volume. Now, his first machine actually -- well, actually, I'll go back in time. So, in the 1950s, he actually attached orthovoltage x-ray machine to a Leksell stereotactic head frame. And it wasn't until the 60s, late 60s, that he started using cobalt-60 as a source. You all are familiar that cobalt-60 has a half-life of 5.26 years, effective energy about 1.25 mV.

And this early machine had 179 cobalt sources in it. And there was an internal helmet of sorts that would collimate the beams of radiation. With time, there was the development of the B units and the C units. And licensing guidance has come out of this committee on those two different machines. And those utilize 201 cobalt sources.

And then most recently, the Perfexion and the Icon units were introduced. These had a robotic couch and cone-beam CT capabilities. They still used fixed sources, which is important for today's discussion.

But advances were made. And they found that 192 cobalt sources worked just fine, in fact provided great distributions. And these particular devices were going to in a sense contrast to the Akesis system so we can put it into perspective, realizing that this group was responsible for providing guidance for these different pieces of equipment.

Now, the Akesis system contains 30 cobalt sources, significantly less. This becomes important when you're thinking about exchanging sources, because the half-life again is 5.26 years. So, there are clearly some advantages to a system like this. There are approximately 6000 curies of total initial source activity. And if you look at the Elekta systems, it was equivalent, about 6000 curies as well.

Now, the Akesis system is paired with an image guidance system that uses reference images to move the treatment couch, the patient's lying in the

supine position on the couch, head is affixed. And the target is basically moved into position.

Now, it really doesn't matter what system you're talking about. The goals of stereotactic radio surgery are always the same. First, we have to delineate a three-dimensional target volume. Then we have to deliver an effective dose of radiation to that target.

And finally, avoid delivering significant doses of radiation to nearby structures. And we can achieve those goals with any of these systems. If we move on to the next slide.

Now, early on, there was -- there were different patterns, different collimating systems. But if we just jump ahead to the most recent ones, looking at the Perfection unit and the Icon unit, they will use collimator sizes of 4 millimeters, 8 mm and 16 mm.

If you go back in time and we started using the earlier models at our center, basically it's the same as the Akesis system, using 4 mm, 8 mm, 14 mm, and 18 mm collimators. Of course, they wear helmets, and these weighed well over 350 pounds. So only a neurosurgeon was capable of lifting them.

But basically, we're kind of now looking

at a system that's very similar to what used to be the case years ago with the earlier models. Though currently again we're using 4, 8, and 16 millimeters, with blocking positions, because you want to be able to shape your beams, spare normal tissue that's going to be in the vicinity of the target.

If you're treating a pituitary tumor and the optic apparatus is in the general area, you really need to use blocks in order to basically carve out the radiation dose to these critical structures. So, 4, 8, 14, 18 millimeters, again, we're very, very familiar with the people who've used other Gamma Knife systems.

Now, unlike the Gamma Knife unit, the source and the collimating system for the Akesis system will rotation simultaneously during treatment to form 30 non-overlapping convergent 360-degree arcs. So, contrast that to the Elekta systems, they're fixed, fixed beams.

The more recent ones use a different configuration, beyond the scope probably for me to discuss that today. But basically, involving sectors. There are eight sectors with 24 sources per sector. If we could move to the next slide.

The principle, again, is always

convergent beams, regardless of the system we use. In this system, all 30 beams are directed towards the target.

This has another aspect to it that we do not see with the Gamma Knife unit to the same degree, and that is the device has real-time, in-line cone-beam CT capability and kV/kV imaging. We do have with the Perfection unit and the Icon unit, they do have cone-beam CT.

It's used somewhat differently, though. This system actually allows interfractional verification. So just an important distinguishing feature.

I thought it would be useful to go over the workflow of the system, and we do need to advance to the next slide. Actually, one more slide, if we could advance it. Thank you.

So, the first thing we have to determine is how we're going to immobilize the patient. All patients have to be immobilized for this treatment. And much like the Icon system, the Perfection system, we can use a mask, or we can use a headframe.

If one is considering doing fractionated radio surgery, then a headframe probably is not the best solution because it's painful to affix a

headframe to the outer table of the skull.

So, the thermoplastic mask works beautifully if somebody wants to deliver treatment to an acoustic schwannoma and do it in five fractions. You just have the patient come back five days, you place them in that type of system, it works great.

If we're trying to treat something that requires exquisite precision, we're treating the ventral intermediate nucleus of the thalamus to treat a movement disorder, you need a significant degree of accuracy. So that's when you really would want to use a headframe.

Now, there is something very interesting about the system, the Akesis system, in the sense it's somewhat of an open platform. It actually allows you to use a Leksell stereotactic headframe. Now, after the headframe is placed or a mask system is developed, the next step generally is to perform some type of imaging CT scan, occasionally, but usually it's an MRI scan.

And then we generate a treatment plan. If we could go back, I think, to the slide, was it before this? The one after that, thank you. Next one, thank you. So, we develop a treatment plan for each patient to get adequate coverage of a target,

sparing normal surrounding tissue.

Again, another interesting point, this is somewhat of an open platform. So, one can actually use a gamma plan to develop your treatment planning. So again, there's a lot of overlap, it shares a lot of commonality. And that becomes important when you're talking about developing license guidance. Because it's not a completely foreign system.

So, we generate basically a treatment plan. We'll move a patient into position. We will confirm patient position, target shape by co-registering CT images or MRI scan images.

And then basically we can go ahead and begin treatment. Occasionally we have to apply some corrections, very, very fine movements in the x, y, or z planes. But then we're ready to deliver the treatment. Next slide. Next slide, please. Thank you.

So once all the treatment parameters are verified and accepted, the control system will automatically execute the plan treatment. During the treatment again, we have online imaging for interfractional verification. This is a little different than what we're used to.

In a Gamma Knife, where you have a

patient motion management system, you can put a little sensor on the tip of the nose and track the patient's motion. And if it gets out of spec, basically the machine stops, it stops treatment.

So, this is a little different. But again, there are many ways one can do verification. It does not have to be with a patient motion management system like the Elekta system. So next slide, please.

So, the first Akesis Galaxy unit is scheduled to be operational this year. It's going to be installed at Case Western Reserve Medical Center in Cleveland, Ohio. And I just contacted the chairman last week to find out if they had a better idea of the time, the date. Unfortunately, we still don't have that information.

The NRC staff has determined that Akesis Galaxy RTi should be regulated under 10 CFR Part 35, Subpart K, or 10 CFR 35.1000. This is similar to the Icon and the Perfection system. Next slide, please.

I really wanted to highlight two areas, training and experience and also physical presence requirements. The reason for highlighting these two areas is simply because this tends to draw a lot of scrutiny from licensees.

Due to the similarities, excuse me, between the Akesis Galaxy RTi and the Elekta Gamma Knife, the subcommittee recommends that the draft guidance be modified to not require at a station for AUs, AMPs, and RSOs who are qualified for Gamma Knife.

Draft guidance recommends training on differences, though, between the Akesis Galaxy and the Elekta Gamma Knife that must include hands-on device operation, safety procedures, and clinical use. Next slide.

Training requirements can be satisfied by completion of training programs by the vendor or by an AU or AMP who's authorized for Akesis Galaxy RTi use. The next slide.

Respect to physical presence requirement. The proposed physical presence requirements are similar to that of high dose brachytherapy and the requirements for both the Leksell Gamma Knife Perfection and the Icon units. Next slide.

The draft guidance recommends the AU and the AMP be physically present during initiation of all treatment. The authorized medical physicist and authorized user or physician will be physically present during continuation of all patient

treatments.

If treatments are interrupted, the AU will return to the console to evaluate the clinical situation, mechanical situation to ensure that treatment delivery is in accordance with the treatment plan and the written directive.

I want to underscore that the subcommittee was exceptionally comfortable with the draft guidance. For the reasons that both in principle and in language, the concepts and the language had been vetted by the ACMUI for the Icon units and the Perfection units, as well as prior machines as well, such as the gamma pod stereotactic radio surgery device, which is considerably different. And that actually has a lot of differences than what we're talking about here.

So, the subcommittee feels that the guidance will be well-received by the licensees because, again, a lot of these and language has been vetted by the ACMUI. Specific comments can be found again in the subcommittee report, which is in the meeting packet.

And finally, the acronyms. Any questions or comments?

DR. JADVAR: Thank you, Dr. Wolkov. Any

questions or comments by the subcommittee members?

DR. ANGLE: This is John Angle. I just want to make sure I understand. So, the physicist and AU must be present for all treatments. And that has been true for the existing legacy units as well. This is just a continuation of existing policy.

DR. WOLKOV: Correct.

DR. ANGLE: Okay, thank you.

DR. JADVAR: Okay, let's see if there's any comments or questions by the ACMUI members. Getting none, we move on to questions from NRC staff. No questions?

DR. VALENTIN-RODRIGUEZ: We don't have any questions.

DR. JADVAR: Okay, thank you. Any questions from the, or comments from the attendees in the room? Okay. We have time, we can entertain remote attendees, any comments or questions?

DR. VALENTIN-RODRIGUEZ: Thank you, Dr. Jadvar. Just a reminder, I've enabled everyone's mics on the virtual room and on the phone. So, you can raise your hand and unmute yourself.

If you're on the phone, you can press star-6 to unmute yourself. Everyone should be able to enable their mics. So, you can use the raise-hand

function, or you can just go ahead and unmute yourself for any comments.

Dr. Jadvar, I'm seeing no comments, no hands raised or no one commenting off you.

DR. JADVAR: Thank you. So, with that we can move on to any motion to accept the report by the subcommittee for approval.

MR. GREEN: I would make that motion to accept.

DR. JADVAR: Any seconds

DR. EINSTEIN: Second.

DR. JADVAR: Okay, thank you. All in favor, say aye.

(Chorus of ayes.)

DR. JADVAR: Any opposed?

(Chorus of aye.)

DR. JADVAR: Thank you. Any opposed? Any abstentions?

Okay, the motion carries, and the report is approved.

Thank you so much, Wolkov, and all the subcommittee members.

Okay, we move on to the next agenda item, number six, which is a review of prescription error reduction methods by Mr. Green.

MR. GREEN: Thank you, Dr. Jadvar.

Good morning. I asked to put a little time on our agenda today to look in depth at a recent medical event.

And I need to provide the caveat, I'm a pharmacist and I will focus on drugs, but there may be some applicability into other modalities of Gamma Knife and intervascular radiology and certainly a perspective from the patient's rights.

My purpose in this activity is not to highlight the institution, the clinicians, or the licensee. But I think it's singular case that we'll talk about today illustrates a common though process with respect to root cause analysis of medical event and possible corrective actions, so it doesn't reoccur. Next slide, please.

During our spring meeting last year, this event was quite fresh and was a subject of discussion amongst members of the ACMUI.

It's reported that two radiopharmaceutical misadministration occurred involving two patients. They were each scheduled to receive 7.4 gigabecquerels, or 200 millicuries, or a lutetium-177 labeled therapeutic radiopharmaceutical. These are all direct quotes

from the NMED report, which is an interesting read. I've got it here.

One patient was to receive Lutathera, which is indicated for treatment of neuroendocrine tumors. And the other patient was to receive Pluvicto, indicated for the treatment of prostate cancer. The Lutathera patient was mistakenly administered the Pluvicto, and the Pluvicto was mistakenly administered the Lutathera. Next slide, please.

So according to the NMED report, what contributed to the event? Again, these are all quotes from that event report.

It states, they were mistakenly administered. Staff at the clinic and at the external radiopharmacy may have had complacency and perhaps they have treated the tasks of that day, such as opening packages, as being mundane and didn't pay much attention to the circumstances. It also cites perhaps a lack of awareness or training. Next slide, please.

Other factors that were thought to contribute to the error include the recentness of handling. It's been a while since the staff had handled these drugs, and the fact that there were

multiple shipments required -- that were required to and from the clinic and the pharmacy and both cardboard shipping cartons looked similar to each other. And the fact that both patients were scheduled to receive the same 200 millicurie dose of their respective drugs. Next slide, please.

So, what were the corrective actions taken? What corrections were put in place to prevent a reoccurrence?

They implemented a new scheduling process so that Lutathera patients and Pluvicto patients are not scheduled on the same day. A second dual verification process where the authorized user must verify the correctness of the radiopharmaceutical was implemented.

Now that we reviewed this medical event, let's delve into some of the processes that might also serve to ensure that all patients, not just Pluvicto and Lutathera patients at this one medical facility, receive the right pharmaceutical for their intended therapy or diagnostic study.

Additional corrective actions that were taken include a reeducation on the proper procedures and that they will verify each patient's identity using at least two methods of verification prior to

administration. Next slide, please.

To do this, I'm going to need to take you on a tour through some literature and published studies that relate to medication errors, or as their known in the pharmacy world, adverse drug events, ADEs.

Since the publication of the Institute of Medicine Report entitled To Err is Human, health systems have adopted to technology and informational systems to improve the medication use process and reduce errors. Next slide.

It has been identified that there are five rights of medication administration. Medication should go to the right patient. It should be the right drug. It should be the right dose. It should be administered by the right route. That would be intravenous or oral or subdermal, etc. And it should be administered at the right time. Next slide, please.

In the pharmacy practice literature, they have identified five medication use phases. These phases include the prescription phase, where the prescriber chooses the correct medication and dose based on a diagnosis of patient characteristics, what other medications they have on board, and possible

allergies, etc.

Next is the transcription phase, where medication is recorded in medication administration records. And that's transferred to a pharmacy. So, there's an opportunity for an error there. Now, the literature is pharmacy-centric, and we could in our minds change this wording to be "transferred from the pharmacy" to "transferred to the nuclear medicine department."

The third phase is the dispensing phase, where the pharmacy staff or nuclear medicine staff retrieve the correct radiopharmaceutical, which is then transferred to the floor to the patient's -- for administration.

Administration phase occurs where the medication is actually administered to the patient. Following up with a fifth phase, which is the monitoring phase.

We are going to see this in nuclear medicine with our new multi-dose regimens of theranostic drugs, five or six of Xofigo and Lutathera and Pluvicto all have multiple courses of therapy. So, we'll see this monitoring phase as well in nuclear medicine. Next slide, please.

So, these are things we talked about last

year when this event first came up and we were discussing it informally. What are some fixes, is there -- what are solutions that could be brought to bear?

Is color coding an effective means? On my citations page, I've identified two communications about color coding of pharmaceuticals.

There's perhaps a minor role that color coding can play that is most effective, for example, to color code classes of drugs that are high risk medications like potassium chloride with a black cap, danger, okay. Or perhaps a range of medications used in a certain medical setting, like an ophthalmic clinic, with different eyedrops.

But color coding for pharmaceutical products should be used with extreme caution, as there are several problems associated with its widespread adoption. For one, there's a limit to the variety of discernable colors available for commercial use. Well-demonstrated color-coding research in other industries indicates that subtle distinctions in color are poorly discernable unless they are located adjacent to each other, okay.

Contrast of background or surrounding colors could also be problematic if a certain color

must be used for patient identification. And of course, clinicians could be color blind, resulting in possible misidentification of color-coded products. This could be the reason that the FDA and the pharmaceutical industry have frowned upon color coding for the most part.

Does scheduling new patients have an opportunity to play here? This sounds like avoidance to me. Let's all do kidneys on Thursday and brains on Friday, and I mean, yeah, that may be a short-term solution, but I don't think that's a long-term solution.

Are there ways and methodologies that can help ensure the five rights of medication use even when a facility does a procedure infrequently? Might there be improvements in the package design or the font size? Might a timeout when the staff pause and reevaluate the patient, the drug, and the dose prior to proceeding? Next slide, please.

So, what are some possible solutions that are in some ways that we could avoid confirmation bias when clinicians might perhaps fail to see they don't have the correct drug in their hands? I'd like to spend some time discussing some health information technology solutions that might play a positive role

ensuring the five rights of medication use.

These include CPOE, computerized prescription order entry, that can reduce errors in the prescription phase and transcription phase. This would provide assistance in ordering the right drug for the procedure and help ensure that there is not transcription made as there would be in telephonic communication where you mishear something, or you've got poor penmanship.

In the radiopharmacy setting, depending on the market and the community, as many as -- as much as 80% of all radiopharmaceutical prescriptions now occur electronically. So, the hospitals set up this system that says when I say bone scan Mr. Jones, I know we're using Tc Meginate or Tc Oxidronate or sodium fluoride F-18. And what's the dose of that drug.

So, it's all in the system so there's no errors. So, it's guidance, CPOE, we get the drug and the dose right, and that's conveyed to the pharmacy. And we don't have transcription errors where I mishear you or I write it down wrong or I've got poor penmanship. So that's a great tool.

Okay, within the radiopharmacy or nuclear medicine department, the use of an IAD workflow

management system can also be very effective. In such a system, bar codes are used to ensure the correct drug product is selected and prohibits any incorrect drug products from being utilized.

You establish a formulary and a bill of materials. To make Tc MDP, I need sodium pertechnetate and a cold vial of MDP. It's also possible to use a bit of normal saline. But I can't use a vial of medronate, and I can't use thallous chloride 201, and I can't use sterile water. So, it has a bill of materials.

As a radiopharmacist, I have to be there, I'm required to be there as the ANP. But I've got five sterile hoods with four tech, pharmacy technicians and me. And the system allows me to exert control into my delegates. Only do the right thing, prevent doing the wrong thing.

Activity maximums, activity minimums, it's all built in the places. IAD workflow management system.

In the hospital pharmacy, they're doing this today gravimetrically, where they know that this antibiotic, one milliliter weighs this many grams, and you weigh the syringe and then you tear the syringe and then you weigh the syringe. And that

helps you know you've got the right drug in that syringe, because can't tell it by looking at it what that drug is.

We've got that beat hands down, we have a dose calibrator. We've got isotopes. I got decay correction of my activity.

In addition, besides the drug preparation process, the system would only allow a Lutathera prescription to be filled with a Lutathera drug product.

The last component is bar code medication administration, BCMA. This is something that is very common throughout the rest of the hospital. I think everywhere except radiology uses BCMA. Is that the fact? That's the case. For some reason it doesn't go past that invisible wall to radiology. We need to bring it in.

Because if we had BCMA, then the nuclear medicine technologist would bar code the radiopharmaceutical, they bar code the patient's wristband, and they'd know this is the right drug for the right patient. And it's the right amount within the prescribed tolerance of the written directive or the physician's prescription. BCMA. It would also document the time of administration. Next slide,

please.

I'd like to spend a little time looking at the Institute for Safe Medication Practices, ISMP, hierarchy of error reduction strategies. Let's start at the bottom of the arrow, the area that requires reliance on humans, human reliability.

These are low leverage, easy-to-implement solutions, but they're also the least effective. These includes suggestions to staff to be more careful. To provide additional information. To provide additional programs to staff and changes to rules, policies, and procedures.

We've heard a lot of that today, haven't we? But it's the least effective, easiest to implement methodology to effect positive change. The middle section as you go upwards on that arrow are the medium leverage error reduction strategies, where there's warnings, alerts, reminders, and checklists.

This is where you could have redundancies like having two people read the label to make sure it's the right drug. We've heard that cited today as a possible solution. You could also go through your procedure manual and standardize them for consistency.

But let's go to the top part of the arrow,

where we're relying not on human reliability, but relying on system reliability. These are the most effective strategies, but they are the hardest to implement.

These would include automation, computerization, barriers, fail safes, barcoding, patient identification, drug identification, and actions that force functions or prohibit wrong functions from occurring.

As we have reviewed these hierarchical strategies, we think back to the medical events where these two patients were each given the wrong drug and where these proposed corrective actions would fall in that diagram.

Recall a discussion, Mr. DiMarco mentioned it and I mentioned it today, where do they fall on this arrow, the proposed corrective actions? They're all rather on the tail end. Easy to implement, but least effective. I think there are ways to do better. Next slide, please.

In a study published in the New England Journal of Medicine by Dr. Poon, there's some very good insight into the effectiveness of barcode technology on the safety of medication administration. They identified that transcription

errors occurred approximately 12% in units that didn't use BCMA or eMAR but were completely eliminated in units that did use it. That's 12% right off the top.

Ordering errors were 39% of all serious medication errors, but they were reduced 55% with computerized prescription order entry. So rather than calling the pharmacist up and telling me, and I hopefully listen to you, and I write it down and I type it in correctly, if it's electronic prescription or entry, where you've got a preprogrammed this procedure requires this drug with this dose and it's all said electronically, boom, a 55% reduction.

Dispensing errors composed 11% of all the serious medication errors, and they were reduced 67% with pharmacy barcode scanning to ensure the right medication is being utilized to fill that prescription.

And last of all in the administration phase. Thirty-eight percent of all serious medication errors were reduced 51% with BCMA, barcode medication administration.

These are some very significant methodologies that provide long-term significant improvement and reduction of medication use errors.

Next slide, please.

Through the use of electronic medication administration records, they resulted in the reduction of 41% of non-timing administration errors. These studies were quite helpful, and they excluded time reduction errors in -- in nuclear medicine we don't give someone an oral tablet every six hours.

In the regular pharmacy world, you're giving a patient an oral tab every six hours. And if they're given late, well, that's an error. Well, we just give typically one shot. Maybe one shot a month. So those are included from this data.

But it's very significant the amount of impact that these higher order corrective strategies can implement.

Most importantly from a patient's perspective, barcode medication administration technology results in the reduction of 57.4% of wrong medication errors, a 41.9% reduction in the wrong dose errors, and an 80% reduction in administration documentation errors. Next slide, please.

The nuclear medicine departments and radiopharmacies can implement different components of health information technology that can significantly reduce the frequency and perhaps the severity of

adverse drug events. We have discussed computerized prescription order entry, IAD workflow management systems, barcode medication administration, electronic medication records.

This is not something that regulators can force adoption to. Well, except perhaps the federal government's mandate to adopt eMAR. But how can we as medical professionals, as practitioners, as patient rights advocates, as licensees, how can we as members of professional societies advocate for the use of health information technologies to help ensure that patients receive the five rights of medication use?

Thank you for the opportunity. Hopefully it's helpful.

DR. JADVAR: Thank you very much, Mr. Green, for that very educational presentation. I have one question. So, you showed that the computerized systems obviously decrease the errors substantially, you know, 80%, 50-80%, something like that.

So, what's the reason for the residual errors? Is that just because they're, for example, the completely wrong drug was entered? For example, instead of antibiotics, somebody got chemotherapy.

Or what was the residual reasons?

MR. GREEN: Are you speaking of nuclear medicine?

DR. JADVAR: Nuclear medicine or in general. Because I don't know if this was --

MR. GREEN: This was done outside of --

DR. JADVAR: Outside, so say outside not nuclear medicine.

MR. GREEN: I have first-hand experience in radiopharmacy and nuclear medicine where we have -- we -- they implemented and used systems that required barcode identification. So, when a drug lot came in cold kit, 30 vials of cold kit came in, they all got stickered with a barcode.

And that was supervised by a pharmacist. So, there were two people that made sure the right drug got put the right barcode on it. Because you can rely on that barcode from then on.

And even a hot vial of Lutathera would be barcoded. Then again, you'll -- so every time a drug selection occurred that was done manually, it was notated, and that was reported to leadership. Someone's picking stuff up by hand. That's an error point.

And so, there are tools that are put in

place. I can't speak to the studies. They were hospital-wide amongst nursing staff. So didn't it involve nuclear medicine. But I think these technologies are out there, they're in the hospital. They're standard of care in the hospital, right, in everywhere except radiology.

I think if we brought them in the radiology and embraced them, they'd be so effective.

DR. JADVAR: Thank you. I guess we don't have our health administrator, Ms. Allen, here today, but that would have been an interesting perspective from her point of view.

Any questions from the ACMUI members, or comments?

MR. OUHIB: Yeah, hi, this is Zoubir Ouhib. I think that BCMA is a great, great idea. But just like anything else, system reliability relies on the human entry. And when human basically get in there, then now you're open the gate for errors.

The other comment that I have is that, you know, the case of the Lutathera versus Pluvicto, for instance. I was just thinking like the old-fashioned way in surgery, if we're doing the right arm versus the left arm, a very simple magic marker

on the patient's hand with the letter P for Pluvicto or L for Lutathera as a quick check would have probably avoided such errors, you know, going to the wrong patient.

Thank you.

DR. JADVAR: Thank you very much for that comment. Any other comments from the ACMUI members? Dr. Angle.

DR. ANGLE: Yeah, John. I just, Dr. Green, very I think helpful, and I think very insightful presentation. Thank you. I think it was very useful.

And I just comment, this may be applicable to other areas, right? I mean, something like this might be applicable to Y-90 administrations, for example.

DR. JADVAR: Very good, thank you. All right, any questions from the NRC staff or comments?

DR. VALENTIN-RODRIGUEZ: I have a question. So, and this is Celimar, a medical team leader. So today in Daniel's presentation, there was a 35.200 event, which we've seen the last few years.

These are very rare; we get one or two max a year. But every year it seems like we've seen one where there's an iodine-123 administration and

the patients get an iodine-131 administration.

In the last few years, a lot of these events, the root cause is some type of ordering system, scheduling system error. And I highlight the event that Daniel talked about today, because this one was particularly egregious in that there were multiple layers of communication between the physicians, the authorized users, the nuclear medicine technologist. They even called the pharmacy at some point.

And the error I think was caught by some of these people, but eventually the patient received the wrong drug anyways. So obviously from the regulatory perspective, you know, we have a written directive and that's what we, from a radiation safety perspective, that's what we are concerned with, that these administrations go per the written directive or the physician's use.

But I wanted to get your opinion on what else if there's any type of communication. I mean, like Daniel said, Katie Tapp is working on an information notice to kind of disseminate these events and kind of communicate corrective actions to the larger community.

But Mr. Green, you noticed that a lot of

the corrective actions are in the easy to implement but not every effective range. So, what can the NRC do, who can we work with to kind of reduce these errors, which are not -- are rare --

DR. WOLKOV: Yeah.

DR. VALENTIN-RODRIGUEZ: But we do highlight. And some of these are abnormal occurrences, so they are included in reports to Congress.

DR. WOLKOV: In that medical event where the patients were administered iodine-131 sodium iodide, instead of I-123 sodium iodide, there should have been no written directive required if they had been given the right drug and the right isotope. And the fault there I think lies in the imprecise use.

I mean, I cringe when someone says I want a HIDA study. That's the name of a drug that left the market 25 years ago. You mean hepatamine diacetic acid? Well, the drug on the market today's mebrofenin. So, let's say that we're mebrofenin, not HIDA.

Rather than saying I want a thyroid study, they should have their, you know, everyone's got a charge master, or everyone should have a procedure master. You should say a thyroid uptake

and scan is I-123 sodium iodide. A typical dose might be 200 microcuries.

Put it in there. Don't just say, Schedule Mrs. Jones for a thyroid study. And that's where you get which iodine do we use.

So again, there are ways to make more precise the systems. And right now, I think that event initiated with a very loose system.

DR. JADVAR: Any other comments from NRC staff? Dr. Harvey.

DR. HARVEY: I just want to thank, this is Richard Harvey, I just want to thank Mr. Green for an excellent present. As others have noted, it was very insightful.

I agree that this is the way we're headed, and this is what we're doing. I think this is the way we need to go. We need to bring it into radiology.

I do like the idea better of, I think Mr. Ouhib mentioned that you know, there can still be errors injected when humans. But I think that, at least my own opinion is that if pharmacy puts the barcodes on.

They're used to this. They do, I think they do a better job of this. And I think the human

errors will go down. And I think it's demonstrated in the data you've shown us.

So, I like moving the barcoding identification to the pharmacy structure rather that in nuclear medicine itself. So, thank you.

DR. JADVAR: Thank you. Any other? Oh, sorry, please, Ms. Shober.

MS. SHOBER: Hi, yes, this is Megan Shober. I just want to point out with the medical event we talked about earlier with the I-123 and the I-131. Ordering an I-123 study does not require a written directive.

And so, you know, when we're talking about delivering in accordance with the written directive, that breaks down with the I-123 studies a little bit.

DR. JADVAR: Yeah, that's correct. Oh, Dr. Tapp.

DR. TAPP: Yes, this is Katie Tapp. I had a question. Why is it radiology not using the barcode system if other people are? Is it possible that maybe our regulation with the labeling or anything by the NRC side, or?

DR. WOLKOV: It's a simple answer, and I'm embarrassed to say this. But in the regular drug

world, every drug has a NDC number, national drug code. Three parts: who's the manufacturer, what's the drug, and what's the package size, three segments of that number. And that will go for any IV drug or any tablet or whatever.

There aren't NDC numbers for radiopharmaceuticals, but there's one for the janitor, one for the cold kit. There's not one for Tc MDP unit dose. There's one for the 1-curie bottle of I-131 sodium iodide, but for the 14-millicurie capsule that's been prepared for Mr. Jones.

But there are ways to jump that chasm and still provide barcode medication administration, patient drug identification, matching pairs, make sure it's the right drug for the right patient.

So, in the rest of hospital, it's seamless because they use the NDC numbers. In nuclear, we're a little different. But you can still accomplish BCMA. It's everywhere else in the hospital, and it should be in nuclear medicine.

DR. JADVAR: Okay, any questions or comments from the attendees in the room? And Celimar, we have time also for questions or comments from the remote attendees, if there is any.

DR. VALENTIN-RODRIGUEZ: Yes, so a

reminder to everyone in the virtual room, you should be able to enable your mic. So, raise your hand and I'll go to you. If you're on the phone, star-6 to unmute yourself.

I see a hand raised. Cindy Luckett, you can unmute yourself.

MS. LUCKETT GILBERT: Thank you for taking my question. I'm an interested party as a nuclear medicine technologist. And I have a -- I'm curious by nature. The barcoding from the pharmacy I think would be ideal as a short-term, if not long-term solution to some of this.

But my question comes from the fact that with the Lutathera, there's three different methods of administration. One is a gravity method, a peristaltic pump or the syringe pump. So that once that vial has its contents taken out of it, how do you tell what's inside? If everything is behind the L-Block in a clean environment, where would the sticker or the barcode go?

DR. WOLKOV: The barcode has to be placed somewhere on the primary container that's accessible. You're not going to put it on the drug vial itself because it's a hot bottle with 200 millicuries in it, so you can't. And that's inside a lead pig, so you're

not going to stick in on the glass bottle itself.

But it needs to be I would say on the face label of the pig. Not on the top, because you might change caps. Okay, so I think a good requirement is to make sure it stays with the -- there's a human-readable label, it's got words and letters, and then there's a computer-readable label. They got to be in the same place.

Right now, we are -- the U.S. nuclear medicine market's a little bit awkward right now because we have drug manufacturers that have brought good drugs to market, but they're using I think the European model where they're familiar with it, where they say here's a bottle of drug, I'll ship it to the hospital. You infuse it. And you have done a gravity infusion method or a peristaltic pump or a syringe pump.

And I think there will be changes in that in the, perhaps in the near future, where you might be able to contact a providing radiopharmacy that says I'd like it in a ready-to-use syringe format for infusion.

Then we may not have dripping lines and puddles on the floor and other events that we have seen. But right now, those drugs are available to

the U.S. marketplace directly from manufacturers, and that may change.

DR. JADVAR: Thank you for your question. Any other questions, remote people?

DR. VALENTIN-RODRIGUEZ: I don't see any other hands. Anyone on the phone, please star-6 to unmute yourself. But at this time, I don't see any other hands.

DR. JADVAR: Okay, very good.

Thank you so much, I think that ends our morning session. We're going to pause for lunch until 1:00 p.m. Eastern Standard Time. Thank you.

(Whereupon the above-entitled matter went off the record at 11:25 a.m. and resumed at 1:00 p.m.)

DR. JADVAR: Hi, everyone, again. Welcome back to the afternoon session of the spring 2024 ACMUI meeting.

And we are on agenda No. 7, Eye90 Microsphere Device Subcommittee Report by Dr. Folkert.

Please.

DR. FOLKERT: Okay. Well, thank you all very much for the opportunity to present our review and commentary on the guidance. So, this is the

comments on the "Yttrium-90 Microsphere Brachytherapy Sources and Devices Eye90 Microspheres Licensing Guidance."

Let's see the Next slide, please. The Subcommittee membership includes Rebecca Allen, Dr. Andrew Einstein, Dr. Darlene Metter, and Mr. Zoubir Ouhib. The consultant to our Subcommittee was Dr. John Angle, and our NRC staff resource was Sarah Spence.

Okay. Next slide, please. Okay. So, on November 3rd, 2023, we were charged by Dr. Darlene Metter to start up the Subcommittee, the Eye90 Y-90 Microsphere Subcommittee, to review and comment on the NRC staff's Draft Licensing Guidance for the ABK Biomedical, Incorporated, Eye90 brachytherapy device for hepatocellular carcinoma.

Okay. Next slide, please. So, just to provide some background for this -- everyone here I believe is quite familiar with how Y-90 therapy works -- but basically, the liver is a primary target for metastatic disease, as well as primary liver cancers.

And these tumors provide a unique target for therapy because they develop this complex tortuous vasculature with very, very narrow blood vessels. That provides a great target for lodging a

physical device to deliver radiation therapy.

Numerous ways of approaching this. Radiation deliveries have been developed, including glass microspheres, resin microspheres, all embedded with a radionuclide that delivers amounts of radiation therapy.

So, the Eye90 microspheres. What they do is it's a glass yttrium-90 microsphere, similar to the Boston Scientific product, that can be directly imaged fluoroscopically, as it's radiopaque during the procedure, using, basically, any x-ray imaging modality. So, it's a similar mechanism to glass microspheres, but it can be visualized at the time of treatment, as opposed to later on, with a nuclear medicine imaging procedure.

The NCR has determined that the Eye90 microspheres will be licensed under 10 CFR 35.1000, similar to other yttrium-90 microsphere brachytherapy devices.

Okay. Next slide, please. So, first off, the Subcommittee did agree that the Eye90 microspheres product does need to be licensed under 10 CFR 35.1000, similar to other yttrium-90 brachytherapy devices. And we do note that the overall guidance for this is very similar to that of

other yttrium-90 microsphere therapies. So, substantially, it's quite similar to the guidance that's been provided previously, and using similar guidance is appropriate due to the similarity of these devices, their indications, and the technical approaches used in their administration.

So, we can move on to the Next slide, please. So, one of the first questions, though, that came up is, as the Eye90 microspheres project is a new device approved by the FDA under an IDE, or Initial Device Exemption, for a clinical trial, there are a limited number of Authorized Users that will be available to provide training. And training is necessary for this because, while it is similar to other marketed devices, it does use a proprietary system for delivery of these microspheres. And so, should there be unique requirements for training in this situation?

So, move on to the Next slide, please. And we recommended, similar to the discussion earlier where we were looking at the new Gamma Knife device, that in-person training is necessary for initial qualification for the Eye90 microspheres product for unsupervised use.

And this training must be hands-on and

conducted in the physical presence of an AU who is authorized for the product. At least three cases must be performed in the presence of this Authorized User.

And the Authorized User may be provided by the vendor for training purposes. So, you can't just substitute an Authorized User who's certified for TheraSpheres or for the SIR-Spheres. It has to be someone specifically Eye90 microspheres product trained, which will cause some limitations because of the number of people available for it, but this is felt to be an absolute requirement for the certification and qualification of this device.

Next slide, please. In terms of documentation, this was a more general observation made by the Subcommittee on the draft. They noted that the dose and activity should be consistent in the written directive and the subsequent documentation. There were some initial comments in the draft version of the guidance that suggested some degree of interchangeability, but we strongly recommend that everything, activity versus dose, be used consistently and using a consistent form of documentation of dose.

Next slide, please. If "dose" is used,

reported dose should indicate absorbed dose to the treatment sites and/or to dose-limiting structures and organs. So, it should be very consistent if you are treating, say, the whole liver, or if you're treating the right lobe of the liver. That should be used throughout, and you should use absorbed dose for the treatment sites.

If you're indicating dose to dose-limiting structures, such as the bowel, such as the liver, again, it should be in terms of absorbed dose to the dose-limiting structure. And the nomenclature should be consistent in this and in other licensing guidance provided by the NRC and the Advisory Committee for the Medical Use of Isotopes.

Next slide, please. Any other questions or comments?

DR. JADVAR: Thank you, Dr. Folkert.

Do you have any questions from the Subcommittee members or comments?

Please, Dr. Harvey.

DR. HARVEY: Hi. Richard Harvey.

I was just curious, does the vendor provide an AU to provide the training for other AUs? Or can another vendor staff member provide the off-register training? Or does it have to be an

Authorized User from the vendor/manufacturer?

DR. FOLKERT: So, it must be an Authorized User who is certified in it. And so, the vendor could, say, perhaps pay for an Authorized User from another site to do it, but they have to provide that person to come to the site.

DR. HARVEY: Richard Harvey again.

So, a non-Authorized User cannot provide this training? Someone from the company cannot provide the training. It has to be an Authorized User?

DR. FOLKERT: It has to be an Authorized User.

DR. HARVEY: Thank you very much.

DR. JADVAR: Any other comments/questions?

DR. FOLKERT: Yes, I'll just make a comment that I struggled with this part of the document myself. Because, you know, you take a new user; this makes perfect sense. You take someone who's done hundreds of TheraSpheres and SIR-Spheres, and really, it's just a little bit of the mechanics are different with the device. And do they really need an Authorized User to be on hand?

But we felt we had to make a document

that applied to everyone. This is the rules we've had in place for the other two devices. And so, you know, this has been the struggle with this. You know, conceivably, if you want to become a site that uses all three, you have to have nine different visits from AUs to be an academic site that uses all three available devices. That's quite a lift, but we didn't see a way around it.

DR. JADVAR: How many centers or AUs are available for this at this time, approximately?

DR. FOLKERT: I mean, it's very limited. I mean, this is being only approved under an IDE for the use in a clinical trial. So, until they are able to get a number of sites going through the clinical trial, there's going to be a very tight bottleneck for AUs specific to this device.

DR. JADVAR: Very good.

Please, Dr. Harvey Wolkov.

DR. WOLKOV: Harvey Wolkov.

I was just wondering about the one slide that said at least three cases must be performed in the presence of an AU. How did you come up with three cases as opposed to five cases? Is there other guidance where it is specified, the three cases?

DR. FOLKERT: Yes. I mean, this mirrors

prior guidance that was used for TheraSpheres, for SIR-Spheres. So, it's for a similar vehicle.

DR. WOLKOV: Okay.

DR. FOLKERT: Yes.

DR. WOLKOV: Thank you.

DR. HARVEY: Richard Harvey.

Yes, and if you look at the NRC 313A forms, they say three cases. So that, again, mirrors the guidance, but also is consistent with NRC 313A forms.

DR. JADVAR: Any other comments?

Please, Ms. Shober.

MS. SHOBER: Hi. This is Megan Shober.

I have a maybe more general question for this. I'm really struggling to understand why this product wasn't just added to the other microsphere licensing guidance. I'm not sure why it warrants a separate, totally separate, guidance.

And I guess the reason for that is, with the emerging medical technologies rulemaking that's in process, these technologies are all going to be underneath the same section of the rule, when that's eventually proposed. So, I don't know why we aren't trying to standardize that now.

DR. VALENTIN-RODRIGUEZ: I can take that

question, if you would like.

So, our process for issuing emerging medical technology licensing guidance under 35.1000 right now is pretty flexible, in that, if we issue guidance for a specific device, we will have to follow other statutes/regulatory requirements outside NRC if we were to do a more generic guidance -- meaning it would be applicable to different manufacturers.

So, by issuing specific guidance for a specific device, we can be more flexible and issue guidance in a quicker manner. So, I mean, right now, since we have the emerging medical technologies, these guidance documents, eventually, licensees can use them maybe as a reference, but they won't be necessary, since we aim to bring new requirements for microsources and microspheres. So eventually, licensees will not have to rely on these licensing guidance documents to license microsphere devices unless it's something totally different that would be outside our regulatory framework.

So, that's really why we didn't take just the TheraSpheres/SIR-Spheres guidance and apply it to more or different types of manufacturers. And I don't have the history on why. I presume it's because they were very similar at some point, where we could

actually bundle them together. Maybe someone from the medical team has the history on that, but that's the reason, for example, Akesis, we issued a separate licensing guidance document and for Eye90 as well.

MS. SHOBER: Yes, to me, it seems like the products are so similar, and, I mean, even the report says how similar they are. And it just feels like a lot of administrative burden and licensing burden to have separate standards for those. So, I mean, I would personally prefer for them to be in the same guidance document. I think it would help on the licensing end, as well as for RSOs that are trying to get physicians through.

DR. JADVAR: I guess one way to think of it is to have it as a class. So, these are all in the same class. As Megan just mentioned, the report says these are already similar technique, methods, purpose. And so, maybe at some point these can be thought of as a class rather than just individuals.

DR. VALENTIN-RODRIGUEZ: Right, and that's when we have to comply with other regulatory requirements, not from the NRC, but, for example, the federal government, where if we issue guidance for a generic class of devices, for example, we will have to go through additional public comment periods and

reviews.

We would have to provide -- maybe; it doesn't mean that we would have to -- but we would have to go through a process to review and ensure that this would not be considered a major rule, and we would have to go through some additional reviews by Congress or OMB.

So, by keeping it as a specific device, we kind of make our process more flexible. We can issue it quicker.

DR. JADVAR: Yes, very good. Any other comments? We heard from both the ACMUI members and NRC. Any other comments from NRC staff?

No? Any comments from the attendees in the room?

And if not, we have time for remote attendees, if they have any comments or questions.

DR. VALENTIN-RODRIGUEZ: As a reminder, anyone who is on the virtual room can raise their hands and unmute themselves. For those on the phone, please press star-6 yourself.

I see Ashley Cockerham. You have your hand raised.

MS. COCKERHAM: Hello. Good afternoon, ACMUI. This is Ashley Cockerham with Mercurie

Consulting.

A quick question. Was there any consideration -- it looked like in the new guidance that there were different medical event reporting or written directive requirements that could be revised orally for the Eye90 microspheres. And this would not be the case for the other types of microspheres?

DR. JADVAR: Who wants to address that?

DR. FOLKERT: Is there a specific portion of the document that you're discussing? I don't remember offhand the specific guidance in that area.

MS. COCKERHAM: Sure. Let me --

MS. SPENCE: Sarah Spence.

I believe, Ashley, you are referring to the provision for terminating the procedure if microspheres are observed depositing in the wrong location. Is that correct?

MS. COCKERHAM: Correct.

MS. SPENCE: Yes. So, that was a provision that was considered specifically for this device because the microspheres are directly imageable on fluoroscopy during the procedure. We may consider expanding that to the other devices in the future during the emerging medical technologies rulemaking, but we have not evaluated those at this

time.

DR. JADVAR: Thank you.

Any other comments from remote attendees?

DR. VALENTIN-RODRIGUEZ: I don't see any other hands raised.

DR. JADVAR: Okay. Thank you.

So, with that, do I have a motion to accept the written report of the Subcommittee?

MR. GREEN: So, moved.

DR. JADVAR: Any seconds?

DR. HARVEY: Richard Harvey. I'll second that.

DR. JADVAR: Okay. All in favor say aye.

Any opposed?

Any abstentions?

The motion carries. Thank you.

Thank you, Dr. Folkert and the entire Subcommittee.

We move on to item No. 8, the Medical Events Subcommittee Report by Dr. Harvey.

DR. HARVEY: Thank you, Dr. Jadvar.

Good afternoon. I appreciate the opportunity to present the Subcommittee's report on Medical Events today.

Next slide, please. Thank you very much

to all of the Subcommittee members: Dr. Folkert; Mr. Green; Dr. Metter, who has now finished; Mr. Ouhib, and Dr. Wolkov, as well as our consultant, Dr. Angle, and our NRC staff resource, Mr. DiMarco.

Next slide, please. The Subcommittee's charge is to review medical events, to advise the Advisory Committee on the medical use of isotopes, and the United States Nuclear Regulatory Commission about emerging trends that may need regulatory attention.

Next slide, please. Background. Quickly, the NRC and ACMUI review medical events that occur throughout the country on a regular basis. Medical events occur when radioactive material use in health care results in unexpected radiation dose to patients. Again, please refer to the regulations.

The Medical Events Subcommittee of the ACMUI reviews the data to analyze the nature of the medical events, identify emerging trends, and provide recommendations to the ACMUI and NRC.

Next slide, please. So, the review period is fiscal years 2021, 2022, and 2023 with the associated dates on the slide.

Next slide, please. A quick summary is that there were two overarching themes: Human error,

which, again, we know we need to say a little bit more about the type of human error. Some of those human errors have been created by poor communication and feedback and failure to work in teams.

Another overarching theme is inexperience. There certainly is a number of new radiopharmaceuticals coming out, and more Authorized Users that may infrequently use some of the radiopharmaceuticals. And this rapidly evolving use of radiopharmaceuticals, and again, this dissemination of use to smaller institutions with lower frequency of procedures performed, can result in additional medical events.

Next slide, please. Specific issues. So, increasing medical events from new and increasing use of current therapeutic radiopharmaceuticals, as well as new ones.

Yttrium-90 microsphere procedures remain the most common medical event. We have seen quite a few medical events involved with yttrium-90 microspheres.

The ACMUI action is that there were two specialty specific Committee members added to the Committee.

ACMUI recommendation: that the

Authorized Users adhere to manufacturer recommendations. We've seen a number of cases where catheter sizes weren't used that were recommended by the manufacturer. So, it's very important to follow the manufacturer's recommendations. This will help avoid aggregation, right, and again, using recommended catheter size and proper needle gauges.

Microspheres need to be agitated to avoid settling or clumping, and this will assist in prevention of aggregation. Users must remain conscientious and adhere to all manufacturer recommendations during delivery of the microspheres.

Next slide, please. So, looking at the data, what we have is 2017 through 2023. And first, we'll look at 35.200, which, if you look at the number, it's been relatively flat. It's peaked at four in a couple of different years, but relatively flat.

A timeout may have prevented all of the medical events in 2021 and 2023. So, we looked at timeouts possibly preventing those in the classification of wrong drug, wrong dosage, and wrong patient. So, a timeout could be beneficial in avoiding these medical events in 35.200.

And, currently, extravasations do not

have a reporting requirement. So, they are not included here.

Next slide, please. 10 CFR 35.300. So again, timeout. Wrong drug, wrong dosage, wrong patient. And for 35.300, a timeout may have prevented 50 percent of the medical events in 2021, 30 percent of the medical events in 2022, and 91 percent of the medical events in 2023, by this definition.

Next slide, please. 10 CFR 35.400. So, we can see here that there were a relatively small number of events, relatively flat. We're not seeing any real trends here.

There were two eye applicator issues, one in 2022 and one in 2023. Not to get too much into specifics, but 2022, excessive eye-rubbing by the patient dislodged the source. And in 2023, there was a shift; the eye plaque shifted, resulting in the medical event.

In 2023, there were also two wrong doses delivered, one where the wrong number of sources were used, and second, where sources were removed early, due to patient's medical condition. So, patient's medical condition necessitated stopping the treatment and resulted in an underdosing.

Next slide, please. To continue with

.400, there is a typographical error, which I apologize for, under 2021. The total, where it says, "Timeout...may have prevented," in the last row, it says two. That number should be three. Okay? So, I apologize for that.

In 2021, the wrong patient was treated. And we see, again, a relatively flat number and no real trend in the number of medical events in manual brachytherapy.

Next slide, please. So, to summarize this section, potentially 23 percent, or 9 of 39, of the medical events from the time period of 2017 to 2023 may have been prevented by use of a timeout. Again, that's wrong site, wrong source, and wrong patient.

So, a timeout or a checklist for 2021 may have prevented 3 out 4, or 75 percent, of the medical events. In 2022 and 2023, there was no benefit to having a timeout.

Next slide, please. 10 CFR 35.600. So, we can see the breakdown, and we can see that the number of medical events is relatively flat, somewhere 10, plus or minus a few.

For the last three fiscal years the most significant causes of medical events seemed to be

human error, which our defined as wrong position, wrong reference length, and wrong dose or source strength, and then, machine or applicator malfunction.

So, 37 of 65 medical events for this period 2017 to 2023, or 57 percent, were from human error in these different classifications. If you break it down, 40 percent in 2021; 75 percent in 2022, and 63 percent in 2023.

For machine/applicator malfunction, 12 of the 65 medical events, or 18 percent, occurred during this time period. That was 20 percent of the medical events in 2021; 18 percent in 2022, and 25 percent in 2023.

Next slide, please. So, this slide breaks down the different procedures into different anatomical locations. And as you can see here, gynecological procedure is the most common site for the medical events. Approximately two-thirds of the medical events were from gyn procedures, which was 43 of 65, or 66 percent. So, certainly, gyn seems to be an area that needs to be focused on.

Next slide, please. All right. So, medical events that may have been prevented by use of a timeout. These are those in the category of wrong

plan or wrong dose.

So, you can see the breakdown there. And in total, 5 of 65, or 8 percent, of these medical events may have been prevented through the use of a timeout.

Next slide, please. The other issue that it was concerned about is infrequent user or inattention, and how conscientious the Authorized User is during these procedures. Again, this is difficult to determine based on the information that's provide in the database, in NMED. Before this assessment, we assumed that wrong position is a surrogate for infrequent user/inattention, and improved training may be beneficial.

So, 20 out of 65 of these medical events, or 31 percent, may have been caused by infrequent use; Authorized Users who are not well-versed in these procedures, and lack of conscientiousness.

Next slide, please. We're now in 10 CFR 35.1000. Here's a medical events summary.

And for the first slide here, we're looking at radioactive seed localizations. And there relatively few radioactive seed localization medical events.

In 2023, as Mr. DiMarco mentioned

earlier, that was due to a delayed seed removal. The surgeon mistakenly removed the surgical clip rather than the radioactive seed. They must not have used the gamma surgical probe to identify that what they removed, what they excised, was actually radioactive. So, certainly, I would think that this is fairly preventable.

Next slide, please. Intravenous cardiac brachytherapy. There haven't been very many of these events, most likely, because this is a -- well, I shouldn't say that. I don't know how common these are, but I would surmise that these are not a high-volume type of treatment. And someone can correct me at the end if I'm wrong.

There was one in 2023, in fiscal year 2023. The radioactive source did not reach the intended treatment site because the Authorized User failed to verify source location. And Mr. DiMarco provided a very good summary of that and the difficulty that the Authorized User had in identifying the location where the source was placed.

Next slide, please. We are now looking at the Gamma Knife now, Perfexion, Icon, and Esprit. So, you can see that there have been very few medical events associated with the Gamma Knife. I think this

is great and I think this is a great modality, and it continues to be used very safely.

Next slide, please. So now, we're going to get into the yttrium-90 microspheres, which, as noted prior, is the most common type of medical event that we see.

Thank you for allowing me to pause.

(Pause.)

DR. HARVEY: All right. So, first yttrium-90 TheraSpheres. And you can see the numbers here, the total medical events for this time period. And there seems to be an increase in 2021, 2022, and 2023. We were down in the low teens, and now, we're in the low 20s. Certainly, we're doing more of these procedures than we have been in the past. As mentioned earlier, we don't have the denominator here to know if we're doing better or much worse. So, I really can't make any conclusion with regards to that.

Wrong dose medical events are assumed to be preventable by the use of a timeout. And that's the first line there.

And the second is 20 percent, greater than 20 percent residual activity left in the treatment device. It is a surrogate for infrequent

use of microspheres and/or Authorized User's lack of conscientiousness.

So, a timeout may have prevented 17 percent, 9 percent, and 5 percent of the medical events in FY2021, 2022, and 2023, respectively.

And failure to deliver at least 80 percent of the treatment activity has resulted in a significant number of medical events in 2021 and 2023, 43 and 50 percent, respectively.

Next slide, please. Now, looking at the yttrium-90 SIR-Spheres, again, we're using the same assumptions, that a timeout could have prevented wrong site and infrequent user/inattention, lack of conscientiousness by the Authorized User, as reflected by greater than 20 percent residual activity left in the delivery device.

A timeout may have prevented 6 percent, 11 percent, and 22 percent of the medical events in FY2021, 2022, and 2023, respectively.

Failure to deliver at least 80 percent of the treatment activity has resulted in a significant percentage, 67 percent, of the medical events in 2023 alone.

In 2021 and 2022, 11 percent were from greater than 20 percent of the activity remaining in

the delivery device. So, 11 percent for both of those fiscal years. Again, this may be due to infrequent users performing the treatments and users not being conscientious during delivery. Again, some of those things are difficult to quantify; we realize that.

Actions to prevent yttrium-90 microspheres medical events:

Ensure familiarity with the mechanics of the yttrium-90 microspheres delivery device and the setup procedures.

Confirm all data and calculations in the treatment plan.

Perform a timeout to assure that all elements of the treatment plan are in accordance with the written directive.

Next slide, please. The next slide illustrates some of the possible elements of a timeout: patient identification; the procedure to be performed; the radiopharmaceutical used; the activity to be administered; dosage or a second check of dosage calculation, and that the written directive and dosage to be delivered are identical.

Other things that could be looked at in a timeout are units of activity; anatomic location; patient name on treatment plan; treatment plan

independent, making sure the second check has been performed; for the HDR, reference length is accurate, and implant site location for radioactive seed localizations.

So, Next slide, please. The next slide just shows the acronyms used in the presentation.

And I'd like to open this up to questions from the NRC or turn it over to Dr. Jadvar, so that he can run the meeting.

Thank you.

DR. JADVAR: Thank you, Dr. Harvey, for that very comprehensive report.

This is open now for Subcommittee questions or comments.

Richard?

MR. GREEN: Yes, Richard Green here.

Dr. Harvey, a great presentation.

On page 23, I would point out that possible elements for a timeout, at least for microspheres, the radiopharmaceuticals would be "or radioactive device," since they are technically not radiopharmaceuticals.

And I think that timeouts can be very effective, but I will not stop flogging BCMA.

Okay. Thank you.

DR. HARVEY: Richard Harvey.

Thank you very much, Mr. Green. That is well-taken.

This slide here, No. 23, was meant to be comprehensive for everything, but your point is well-taken and is correct. Yttrium-90 microspheres is considered a radioactive device, although it's more of a radiopharmaceutical therapy; just the way it's delivered is through a device.

So, you are 100 percent correct, and I appreciate that. I'll modify my slides in the future. Thank you.

DR. JADVAR: Thank you.

Any other comments or questions for the Subcommittee members?

Josh?

MR. MAILMAN: Hi. This is Josh Mailman.

And I don't know which number of slide it was again. We've heard this theme a little bit before about lower-usage sites or smaller facilities who do things infrequently. Do we have a cutoff level of what that means for what an infrequent use site is?

And also, does it correlate to the data you showed on whether it was infrequent use? You had some data on infrequent use, and I'm curious if it

correlated to the actual size of the institution that was doing it or what's the measure of infrequency?

As a patient advocate, I think about this, of where I choose to go have therapy. And I'd like to make sure we're precise about it. So, that's my question: how do we choose that precision, and have we correlated the data?

DR. HARVEY: Richard Harvey.

In response, Mr. Mailman, to your comments, we don't have a good handle on what infrequent use is. We don't really have that data. We don't know what different licensees, different organizations, how many of these procedures they were doing. We have kept that as a theme.

We make some assumptions that that is probably the case. And I have chosen to, at least to this point, continue to use the Dr. Ronald Ennis methodology that's been used in the past.

So, I think that, going forward, the intent for the Committee is to take another look at this and decide how we want to do this. Because, as you mentioned, it's very difficult to quantify, and we're trying to be consistent with what has been done in the past. But it doesn't give me a lot of level of comfort because we don't have the information that

you're talking about.

It's very difficult to say or ask or find out how many procedures that these different institutions may be doing. So, it is sort of a "jump to lightspeed" when we're making the assumption that licensees that don't do that many of these procedures may have the ability to have more medical events, but it's also possible that a licensee that does a low number of medical events is very conscientious because they don't do it very often and do a very, very good job.

So, the choice was made by me to keep consistent with the prior methodology, and then, go ahead and maybe make a change going forward. Because it is very difficult to quantify, and I feel very uncomfortable making some of these assumptions without having data to support it. So, I really appreciate your question, and that is the plan going forward.

Did I miss anything for you, Mr. Mailman? I'm sorry.

MR. MAILMAN: I'm going to say slightly, because we do use it when we're listing off reasons, whether it was human error, or whatever, or infrequent use. So, we must have some idea what

infrequent use means if we're going to list it the same as human error.

But then, to extrapolate that onto not necessarily smaller centers, but centers who don't perform or lower-usage centers, I don't think we can make that leap until we define what a lower-usage center is, and then, see if the infrequent usage correlates to our idea of what a smaller center or a lower-use facility is. And then, I think we can make that inference.

But, right now, we are using it as one of the reasons in tables, and then, applying it to a class of organizations that it may or may not be appropriate for. We're making a lightyear jump or just a jump into a different set of realities.

And I would say, having an infrequent usage thing is fine, because that may be absolutely correct, but, then, until we can apply it to what size, and we can list them by how many therapies they do per center, until we do that, I think it's -- because it gives me the impression, as a patient, that I need to ask, "How many of these do you do?" And if the number is low, I'm going to make their numbers even lower, because I'm going to walk.

DR. HARVEY: Richard Harvey again.

Mr. Mailman, I concur, and this might be something that we omit or change for the future, as mentioned. We have to come together, I think, as a committee and make a determination on this. And I think it is very difficult to say what is a low amount of use. And again, if you are doing infrequent use, you might be doing it very well.

So, it is something that we have wrestled with. I won't go into exactly all the specifics as to why we haven't made this change, but we have discussed it and do plan on taking some time before the next evaluation to take a good look at this as a group and come up with a consensus to make a change.

And just out of respect for Dr. Ennis, and sort of what has been done in the past, I have continued on with the methodology. And since it wasn't really devised by myself, I have some uncomfortability with it, and for the reasons that you mentioned.

So, I very much appreciate your comments, and I think it is very important to patients. And again, I don't think this is intended for patients to choose their center, but maybe it's important or maybe it's something that you, as a patient advocate, could tell me differently about.

Thank you.

MR. MAILMAN: Personal note. When I was diagnosed in 2007, I called up where it was recommended to me, and the scheduling tech actually said, "Wow, we haven't done one of these in a long time. I'm looking forward to ordering this and seeing how this goes." It's accurate.

DR. HARVEY: Mr. Mailman, I --

MR. OUHIB: This is --

DR. HARVEY: I'm sorry, Mr. Ouhib, bear with me for one second, please, if you don't mind.

I certainly appreciate that, and I certainly agree with patients taking a very active role in their care.

And so, if what we can do here in the ACMUI and this report, if we can do something as a service to patients, then we want to do that. And we are taking your comments under advisement and look forward to developing a better product in the future.

So, thank you very much for your comments.

MR. OUHIB: This is Zoubir Ouhib.

DR. JADVAR: Zoubir, you had a comment?

MR. OUHIB: Yes, yes.

I think Mr. Mailman brings a very good

point but let me just sort of like an FYI. The ASTRO has looked at this several years ago. And they encourage users to actually create some sort of a center of excellence.

And that is, if you are not doing as many cases, whatever that is, the modality, it is to refer them to a center of excellence. So, that means a center that's doing quite a few of those cases. And they pushed for that, and I don't know what the status of that is at this point.

The other item that needs to be kept in mind is access to a patient also. So, yes, maybe this institution is not doing many cases, and as was mentioned, that institution might very well be a good one and they're very capable of delivering a good treatment. You know that patient doesn't have to travel a long way for a half-hour procedure, or whatnot. And I think that we need to keep that in mind also.

DR. JADVAR: Okay. Dr. Folkert?

DR. FOLKERT: Yes, just to kind of add to that, there are accreditation programs being set up by most of the major professional societies. SNMMI, ACR, and ASTRO, they all have, or in some cases already have in place, accreditation programs for

radiopharmaceuticals which will have some form of center of excellence designation. I know ASTRO is trying to figure out what that number is right now, for the number of cases. SNMMI, I think has one, already has it now.

So, the professional societies have taken that on, and that might actually be the best place to have that number set.

MR. GREEN: Right, but it shouldn't -- I'm sorry.

DR. FOLKERT: No, go ahead.

MR. GREEN: I shouldn't say I love the center of excellence idea. I personally don't because, as a patient advocate who wants to see access across the board, it starts funneling patients into specific areas and specific places, and doesn't provide, I'll just call it, "pancake coverage," "blueberry pancake coverage," where the blueberries are randomly all over, as opposed to just specific single points around the country.

So, I hope what Dr. Harvey can come up with is something that says, for those who are going to do a specific -- this is how to do refreshers; this is how to do whatever you need to provide patient care, and that we don't go into this siloed world

where, you know, if I'm a patient in Montana, I think I'm screwed.

And so, that's my challenge with COEs, is they're kind of siloed care, and as we get out farther, you know, I want good standard of care wherever a patient shows up, not just whoever filled out the forms and did the thing and has enough. I'd like to see great standard of care across the board.

DR. JADVAR: Excellent discussions. And very interestingly, I actually wrote exactly the same question. Josh already beat me to it and asked.

Because I was wondering, when you get these medical events reported by the licensee, is it possible to find out from where they are how many of these are they doing? So that you have a denominator.

Let's say, you know, we had a medical event. I'm at Institution X, and this is the number of exact procedures we do over a period of time, in one year. And then, my question was: maybe if that information is provided at that time to the NRC, just a number, then we can find out -- you know, to his question -- if there is a difference, really a difference, between smaller institutions or smaller clinics, private practice clinics, versus community hospitals, versus academic centers, and if that makes

a difference, and come up with some sort of a definition for that infrequent use and what it means to a patient, actually.

DR. HARVEY: Richard Harvey.

So currently, we don't have that information. I would ask the staff resource, either Mr. DiMarco or Dr. Valentin-Rodriguez, if they might be able to comment on that. Could we obtain that information through NMED or in some other way? Or is that not possible?

Thank you.

DR. VALENTIN-RODRIGUEZ: This is Celimar with the medical team.

So, right now, we don't have any requirement for licensees to disclose how many procedures they do for a certain modality each year. We have performance-based inspection programs, which means that we don't look at all documentation. So, if a hospital does a certain amount of 35.300 administrations that require written directive, we wouldn't go through each of them. It's more of a investigate, talk to people, pull a string. So, in that sense, there's no regulatory requirement for us to ask licensees to provide us with that information.

So, what we do have is training

experience. And what I'm hearing is -- and I'd like to ask the question to the members -- is: are our T&E regulations sufficient to address maybe Authorized Users who get off a license; they don't practice for a number of years?

Is there an opportunity here to include more specific requirements for continuing education? One of the things we're doing right now is asking the ACMUI to take another look at training and experience requirements for emerging medical technologies.

So that we could avoid the type of situations where we have someone who becomes an Authorized User and hasn't performed or hasn't received any sort of training on a certain procedure since they obtained their board certification or became an Authorized User through the alternate pathway.

DR. FOLKERT: Isn't there still a recentness-of-training requirement of seven years?

DR. VALENTIN-RODRIGUEZ: Yes, by continuing education. That's 10 CFR 35.59, yes. Thank you for correcting my wording.

DR. JADVAR: And a lot of these are credentialing at the specific place you are. So, you are not allowed to do Y-90 in first years, right,

unless the hospital credentials you to do it? And they go by continuing education, number of procedures performed, and things of that sort. Right?

DR. ANGLE: This is John.

I can just talk to my own experience. You know, at least in Virginia, it's the certification is pretty much, as an Authorized User, is pretty much without limit. And so, the CME is really a comment upon the Authorized User. I don't know how it's done in other states.

MR. OUHIB: This is Zoubir Ouhib, if I may.

I think the number of cases might very well be a misleading number. Let's just take an example of an institution that's very well-known, well-respected, and they do tons of those cases. But it just happened that one of their users does one every six months, or whatever. So, that could be misleading information.

I think we need to dig in furthermore into this to see what can be done. I mean, I like the idea of a specialty. In other words, a user, within an institution, there's one user that is really dedicated to that type of procedure, and therefore, will be doing the majority, if not all, of

those cases to maintain that expertise.

DR. JADVAR: Thank you.

Dr. Harvey, you had something to say?

DR. HARVEY: Richard Harvey.

Yes, I think that we have to meet the guidelines of training and experience. We have to be compliant with the NRC 313A applications. And that at least currently dictates Authorized Users becoming credentialed and privileged within the organization, to your point, Dr. Jadvar.

So, you know, I don't know; it doesn't seem like we're -- I don't know if we can get our arms around this data, if we can really find out how many procedures are being done by each institution, so we can sort of make these judgments.

So, we may have to go a different way and omit this infrequent users/inattention, because, in a sense, it may not be fair. If we can't get the data, it should probably just fade away. So, I think that's my opinion.

I don't know if we can get that data or not. And I'm just looking to the NRC staff to tell us if we think we could pursue that or if it's just not data that we're ever going to be able to obtain.

So, thank you.

MS. SHOBER: Megan Shober.

I can only speak for Wisconsin, of course, but we have four major medical centers that do Y-90 therapies multiple times per week. And then, there's a big gap after those. And essentially, most of the rest of our Y-90 licensees are doing between, like, one or two a month maybe. And so, there's a huge frequency gap with that.

And I would say, again, only speaking from what I know, in terms of medical events, the vast majority of them are happening at the smaller hospitals.

DR. JADVAR: Thank you.

I guess, again, talking about numbers of similar procedures that are being done at institutions, different places, perhaps -- I know it's not a regulatory requirement -- but perhaps numbers of procedures done by that licensee who reported the medical event.

So, I'm Dr. X. I do 500 of these a year, per year, and now, I have this one medical event that I am reporting. At my institution, 2,000 are performed by others also. So, something like that. If those numbers become available, perhaps we can wrap our arms around this, and again, get to the

question of what "infrequent" means, if it means anything.

MS. SHOBER: Dr. Jadvar, this is Megan Shober. One other comment on the frequency.

So, the hospitals that are performing the Y-90 microspheres, they're inspected every other year. And I would say the inspectors have a really good pulse on the frequency for how many times those sites are doing these procedures.

If we prefer, you know, if a place is only doing one a month or something, we're going to be looking at every single one of those written directives on our inspections. And there really are very few places where we aren't looking at most of the written directives.

So, I think that number is -- I think we have qualitative information that's easy to access, but I think quantitative information would be hard to come by.

DR. JADVAR: Thank you.

Any other comments or questions?

Dr. Harvey?

DR. HARVEY: Again, I just want to reiterate the question to the NRC staff: is there any way we could obtain this data, or not really, and

just omit this going forward?

Thank you.

MR. OUHIB: This is Zoubir Ouhib.

I think the next question that comes up -- so, we have that data. What are we going to do with it at that point?

As we all know, NRC cannot, basically, dictate medical practice. In other words, are we going to tell this institution that you can't be performing this procedure? No, NRC cannot do that.

And I think we need to think about, once we have that data, where are we going with that?

DR. JADVAR: Well, I think once we have the data, I guess we understand the problem better. You know, I'm not suggesting, or we are not suggesting the NRC to change their practice. And, yes, they shouldn't interfere with medical practice. But at least we understand exactly what we are looking at. We exactly would get a sense and pulse of the problem. That would be useful to everybody and to the community.

Dr. Tapp, and then, Melissa.

DR. TAPP: This is Katie Tapp.

I think getting the information, especially quantitative information, would be

difficult for us. The regulations in 10 CFR 35.3045 are very specific on what information needs to be provided for a medical event. And those regulations are very specific to that medical event.

So, even reaching out and saying, "How many do you do in this area?" would be going beyond the regulations, which is difficult for us to ask those types of questions, especially individual licensees, or even asking the states. We would need to get -- it's almost like a survey. So, we can do that under, like, an OMB clearance, but there is a process, and we really need to be knowing what we're doing with the data; knowing the risk-based, and that would be a long process to gather this information, but it's not impossible.

Another way about this, too, it would still require us to ask, but manufacturers know where their products are going. So, I do know one of the yttrium-90 manufacturers has looked at this as well, and I think provided the ACMUI Subcommittee back then -- I just don't have the exact data today. And they didn't believe they saw a correlation between size of an institution or how many vials they shipped there versus medical events.

But this is one manufacturer, and I do

know they provided training to the infrequent -- the places that didn't use it as often, or they'll have a manufacturer representative present. So, they have additional people there. And again, that was just one manufacturer, and I don't have the data here today.

But there may be an ability to go out and ask those questions, but we're talking about a long-term process where we need to know what you would be doing with the information, and we would probably need a recommendation to start a process like this. This is not something we can just simply go out and ask our inspectors to follow up on, at least in the NRC states, because it is not a requirement. It might come from the Agreement States, but not the NRC.

DR. JADVAR: Thank you very much. That was very useful information.

Okay. Now, Melissa Martin.

MS. MARTIN: Right, Melissa Martin.

One question I had, and that's what I was wondering if Ms. Shober might have an idea: when you take this data, one of the questions that's not asked is "What type of institution it occurred at?" That seemed like, I mean, you're collecting all the data for these events. I guess my assumption was that it

would be pretty straightforward to decide whether that's a major medical center, you know, under 500 beds. Just classify it. Or is it happening in office settings? You know, I thought that would be a fairly straightforward way to get the data.

MS. SHOBER: Yes, this is Megan Shober.

I agree with Melissa. I mean, we had -- what? -- 33 events last year. And I think it would take less than an hour of quick internet searching to determine if a site is a major medical center or not. So, I think we can get that pretty directly, and that would be a proxy, of course, for frequency, but in my experience, those major medical centers are the ones that are doing a bunch of them. So, I think your risk of mismatching is pretty low.

CHAIR JADVAR: Okay. Great discussions. So, I think NRC staff has spoken, the Subcommittee and the Committee has spoken. Let's see if there's any comments from the folks in the room.

(No audible response.)

CHAIR JADVAR: If not, we have still time to have -- see if there's any remote questions or comments on this topic.

DR. VALENTIN-RODRIGUEZ: For those in the room, if you need -- if you want to provide a comment

on this topic, please raise your hand and un-mute yourself. If you're on the phone, press *6 to un-mute yourself.

(Pause.)

DR. VALENTIN-RODRIGUEZ: I don't see any hands raise, Dr. Jadvar.

CHAIR JADVAR: Thank you very much.

So, with that, do I have a motion to accept the Subcommittee report?

MEMBER GREEN: So, moved.

CHAIR JADVAR: Any seconds?

MEMBER EINSTEIN: Second.

CHAIR JADVAR: Thank you. All in favor, say aye?

(Chorus of aye.)

CHAIR JADVAR: Any opposed?

(No audible response.)

CHAIR JADVAR: Any abstentions?

(No audible response.)

CHAIR JADVAR: The motion carries. Thank you so much.

Thank you, Dr. Harvey and all the Subcommittee members.

We move onto Item No. 9, Medical Team updates. And this is presented by Dr. Valentin-

Rodriguez from NRC.

DR. VALENTIN-RODRIGUEZ: Good afternoon, everyone. My name is Celimar Valentin-Rodriguez. I'm the Medical Team leader here at the NRC and today I'll just be providing updates on ongoing efforts and activities and initiatives within the Medical Team.

Next slide, please? So today my talk will be kind of broken down into three major focus areas. One of them is rulemaking, which I'll start with. Then I'll go into guidance development efforts and then I'll round out that discussion with other efforts that we're tackling right now.

Next slide, please? So medical rulemakings. Next slide, please? I'm sure we've talked about these two rulemakings during today's discussion. Extravasations rulemaking, which we started in February of 2022, if you'll remember we received a staff requirements memorandum in December 2022 from the Commission directing us to proceed with rulemaking on this. And in the next slide I'll have more of a timeline and I'll get into what these efforts are.

The other major medical rulemaking that we have currently right now is the emerging medical technologies for rubidium-82 generator rulemaking, or

as we refer to as our EMT rulemaking. Ms. Shober was the ACMUI Subcommittee chair on the subcommittee that reviewed the regulatory basis for that rulemaking which we've already issued for public comment. And so, I'll be talking about that as well. So those are our two major ongoing medical-related rulemakings right now.

Next slide, please? So, for extravasation, like I said, in December 2022 we received that staff requirements memorandum. And besides including reporting of certain nuclear medicine injection extravasations in 10 CFR 35.3045, the Commission also directed us to study ways to reduce reliance on patient self-reporting, examine whether we should require that licensees have procedures in place to detect and report extravasations medical events. They also tasked us with looking into whether we could accelerate our rulemaking schedule without shortening our public comment periods. And finally, they also directed us to develop a medical event regulatory guidance, basically regulatory guidance for all reporting of all medical events including extravasations.

Next slide, please? So, in January 2023 we -- February 2023 we established a Joint NRC

Agreement State Working Group to tackle this rulemaking. I think you all received an update sometime last year which was close to our April 19th date where we issued a request for information in the Federal Register notice where we also issued preliminary proposed rule language as part of that request for information. We also had a number of questions out there for stakeholders to provide comments on.

That closed sometime in the summer, and we received over 200 comment letters related to both the preliminary proposed rule text and also the different questions which related to procedures, patient self-reporting, definitions, and other topics.

So, we are on course to provide this proposed rule package to the Commission in August of this year. Currently the ACMUI has established a subcommittee to review the draft proposed rule package which obviously includes the proposed rule. It also includes the regulatory guidance for reporting of all medical events and also includes a draft model procedure for detecting and reporting extravasations.

And we hope to have a teleconference sometime in the

end of May, beginning of June to discuss that Subcommittee report.

And then finally, once we provide that proposed rule package to the Commission and they get a chance to vote on that, we'll published the proposed rule package for a 90-day public comment period. And then the final rule will be issued to the Commission 12 months after that public comment period closes. So, there's some flexibility. There's some uncertainty at the tail end of this schedule just because it depends on when the Commission votes on the proposed rule so that we can issue it for public comment.

Next slide, please? So, the next rule I wanted to discuss was the EMT rulemaking. I think we fairly -- we basically discussed this when the Subcommittee reviewed the regulatory basis. So, this is our major revision to Part 35 which will take a lot of those well-established emerging medical technologies in 35.1000 and basically codify requirements for their use in other sub parts of Part 35, and obviously also including requirements for rubidium-82 generators which we've had an enforcement guidance memorandum in place for a few years now, maybe -- not a few years. Maybe a decade.

And so, some of the proposed changes are here. And many of you saw an extensive 100-plus page regulatory basis which included many of the requirements which we would need to update to bring in those technologies into Part 35.

Next slide, please? So that SRM we received in 2022, but when we received the staff requirements memorandum for the extravasation's rulemaking, we delayed the issuance of the proposed rule for this rulemaking to address the extravasations proposed rule first. So that's while you'll see kind of a big gap between the proposed rule scheduled for this rulemaking and one, we initiated work on that.

So as part of that rulemaking, like I mentioned. last year in the summer, in July we published the regulatory basis for -- I think it ended up being 165-day public comment period. We received over 20 comment letters on that. And our proposed rule with the draft implementation guidance is due to the Commission by winter 2026, which means early, first few months of the year in 2026.

So, one of the things we're planning to do probably is to do some workshops, one or two, with stakeholders as we move into the proposed rule

schedule so that we can address certain questions from the guidance that we got in the regulatory basis which we are evaluating right now. And then just like with extravasations, once that proposed rule is published, we'll do a public comment period, and the final rule will be due to the Commission 12 months after that public comment period ends. So, we're looking at most likely a decade of medical rulemaking covering proposed rules all the way to implementation.

Next slide, please? So, in terms of guidance development, we are -- next slide, please -- as you all saw today with the three emerging medical technologies, licensing guidance documents that you all reviewed and commented. We are keeping up our efforts to try to maintain our fingers on the pulse of EMTs.

And so last year we issued two memoranda for different technologies. These we determined didn't have to be licensed under 35.1000 and could be licensed under existing regulations. CivaDerm under 35.400, which is temporary radiation therapy, and then Technegas which we issued -- I want to say the memo earlier this year. They're both on the Medical Toolkit, and that was for a functional long imaging

agent.

And then of course you'll see the three medical devices that you all discussed today: Akesis, Eye90 Microspheres, and Liberty Vision, which once we address your comments, we'll be able to issue as final and post to the Medical Toolkit.

One of the other types of technologies that we're looking into right now is thorium generators. As you all know, there's a big buzz with alpha therapies and beta therapies that are being -- there's a lot of clinical trials that are ongoing, and so one of the questions that we've received from our stakeholders and our licensees is that we don't have guidance for these therapeutic generators for therapeutic radionuclides. And so, thorium-228 basically. We've seen other generators such as generators for lead and other types of alphas that are coming down the pike. So, we want to make sure that we review the use of those since they'll probably be going to nuclear radiopharmacies first.

And of course, we're looking -- we're keeping track of a few new microspheres that are not Y-90 and we are also keeping track of various alpha therapies that are in advanced stages of clinical trials, obviously one of those being actinium-225 and

like I mentioned lead-212, which are the most advanced and look to be the most promising.

Next slide, please? Another guidance development effort that is ongoing is our training and experience implementation guidance. We started developing this guidance in response to Commission direction in what we call the T&E paper, which received a staff requirements memorandum back in January of 2022.

This training and experience implementation guidance is not to address -- does not change any requirements, but it merely provides additional information for licensees and for our staff in Agreement States and at NRC when reviewing training and experience licensing actions. So, I know that in the past we've talked a lot about the different pieces of your T&E regulations including preceptors, documentation, the different between hours, work experience, class and laboratory training, supervision.

And so, our Training and Experience for All Modalities Subcommittee is currently reviewing this guidance and we hope to have a subcommittee -- a public teleconference -- not a subcommittee -- meeting sometime in May to review the ACMUI spots on

this guidance.

Next slide, please? The other big guidance development project that we have ongoing -- not development, but update is Regulatory 8.39, Release of Patients Administered Radioactive Materials, Revision 2. As a reminder, back in the summer of 2023 -- maybe it was April -- we issued DG 8.61 for public comment, which was our revision to Reg Guide 8.39. An ACMUI subcommittee provided a report on that draft Reg Guide back in December of 2021.

Next slide, please? So as part of our process we issued the Draft Regulatory Guide for public comment in April, and we received over 60 comment letters from a number of different stakeholders including Agreement States, professional societies, federal agencies, and others.

So currently we're updating the Reg Guide based on these public comments and we're talking all those comments seriously. And we're also developing a regulatory analysis that includes a cost-benefit analysis to ensure that we're looking at the burden of this Regulatory Guide from the perspective of licensees. The initial regulatory analysis that we published with the Draft Regulatory Guide was from

the patient perspective.

And so, we are working on that cost-benefit analysis and expanded regulatory analysis and we hope to provide the revised Draft Regulatory Guide to you all for another review of -- for another chance to review before we issue it for public comment again. And as part of that we'll also provide the regulatory analysis since we have some assumptions for costs and burden in that document.

Next slide, please? Medical events. I think I talked a little bit about this previously, but as part of the extravasations rulemaking we're also developing its own stand-alone Regulatory Guide for reporting of all medical events. I think I mentioned that as part of that Regulatory Guide we tried to incorporate those best practices on reporting medical events that we issued as part of the NMED annual report a few years back. And so, as part of the extravasations rulemaking you'll see a new Regulatory Guide for all medical events. Obviously, there's also information there about how to report extravasation medical events based on our reporting criteria.

And then the other part of that that's also been mentioned today is that we have been

developing an information notice to share information about radiopharmaceutical-related medical events, and we plan to issue that later this year. Last year you all received a presentation from Dr. Katie Tapp about recent radiopharmaceutical-related medical events and we've had a lot of discussions today about those types of events.

Next slide, please? Other efforts. Next slide. Thank you. So, we continue to answer a lot of training and experience questions related to the American Board of Radiology's termination of NRC recognition. Back on November 30th of last year we published an information notice which aimed to provide more information about the existing regulatory framework for those who are planning to get an ABR Board certification or those who already have one. And by those, I mean individuals.

And so right now we don't have any changes planned toward training and experience regulatory framework, but as always, we're open to suggestions and we're open to your feedback. Ms. Maryann Ayoade has been doing a lot of outreaches to professional societies and just individuals who keep sending us questions.

I don't know, Megan, if you've seen a lot

of questions in Wisconsin about that, but we've certainly seen an uptick here at the NRC.

So, we continue to answer those questions. And like I said, we don't have currently at this time any efforts to update or revise the regulatory framework for T&E based on ABR's termination request.

Next slide, please? So, with regard to household waste, as Lillian mentioned at the beginning of the meeting, a few years ago the ACMUI recommended that we assess the issue of detection of short-lived medical isotopes in municipal waste. And this is basically from released nuclear medicine patients. We did send a voluntary survey to the Agreement States requesting information on best practices and the need for additional guidance.

The other thing that we are doing is assessing our regulatory framework, seeing where we've done risk assessments to -- based on the different types of waste classifications that the NRC. And we're also using that information to develop recommendations. So, in the fall you'll all receive a presentation. We're also developing a paper that we might share with you all with those recommendations.

So, we plan to close that item pretty soon.

Next slide, please? So, I think that's it for me. If you have any questions about ongoing rulemakings or guidance development efforts, please let me know or reach out to any member of our team. With respect to emerging medical technologies, we're always looking for the next new item, so if you have any information about new technologies that you're hearing about, please let us know. We interface a lot with Dr. O'Hara and his team and the folks over at Cedar to try and get ahead of the game.

So, with that, I close my presentations and open it up to the Committee for any questions.

CHAIR JADVAR: Any questions from the ACMUI? Mr. Green?

MEMBER GREEN: I know you didn't speak to it, but on your EMT page you have depicted the NorthStar RadioGenix System, which has been withdrawn off the market.

DR. VALENTIN-RODRIGUEZ: Yes, I think we -- that graphic was just pre-RadioGenix.

MEMBER GREEN: Good.

DR. VALENTIN-RODRIGUEZ: Yes. But we were in contact with Megan and the state of Wisconsin on that pretty early. So, yes. But we also plan to

use the -- I wanted to add that we're planning to use that as operating experience to ensure that if there was another technology similar to RadioGenix at least we have guidance and we can use that as kind of a baseline to provide requirements for the future technologies. And we're doing that for example with U-Ray and other technologies that are no longer on the market.

CHAIR JADVAR: Great. Thank you. Any other comments from the Committee members? From the NRC? Your colleagues.

(No audible response.)

CHAIR JADVAR: Anybody in the room? Yes, Ms. Shober?

MEMBER SHOBER: Yes, this is Megan Shober. I think with those thorium generators that would be a great topic for the fall meeting. I personally don't know a ton about how those work.

DR. VALENTIN-RODRIGUEZ: Sure. We'll take back. Thanks.

CHAIR JADVAR: And maybe we can -- we have a little time if we want to get remote attendees, if they have any comments or questions for Dr. Rodriguez' presentation.

MS. ARMSTEAD: I don't see any hands

raised.

CHAIR JADVAR: Okay. Excellent. Thank you for that wonderful presentation.

DR. VALENTIN-RODRIGUEZ: Thank you, everyone.

CHAIR JADVAR: So, we're going to pause until actually 3:30. And remember, there's an eclipse out there, so don't look at it directly. But we'll be back in this room at 3:30 Eastern Time. Okay?

Thank you. Bye-bye.

(Whereupon the above-entitled matter went off the record at 2:23 p.m. and resumed at 3:29 p.m.)

CHAIR JADVAR: Okay. So, let's get started. I hope for people who were here they were enjoying the magic of nature, the sun eclipse. It was wonderful.

We move on with our agenda items here. No. 10, Liberty Vision Y-90 Episcleral Brachytherapy Source Subcommittee Report by Mr. Ouhib.

Are you on?

MEMBER OUHIB: Yes, I am.

CHAIR JADVAR: Okay. Wonderful.

MEMBER OUHIB: Thank you. Thank you. Okay. My name is Zoubir Ouhib. I'm a therapy and

medical physicist and I'm here to present to you the recommendation from our subcommittee regarding the NRC staff Draft Licensing Guidance for the LV Liberty Vision yttrium-90.

Next slide, please? So, in our agenda we'll talk briefly about the subcommittee membership, our charge, the background of this device, a description of the device, and then recommendation and general comments.

Next slide, please? This is our members. I don't think I need to go over that.

Next slide, please? Okay. The ACMUI Chair, Dr. Darlene Metter, appointed this subcommittee to review the Liberty Vision technology and comment on the NRC staff Draft Licensing Guidance for the LV Liberty Vision Corporation Yttrium-90 Disc and iWand Ophthalmic System. Let me just say that the report of the subcommittee was submitted, and NRC staff has determined that this product needs to be listed under 10 CFR 35.1000.

Next slide, please? So, the ophthalmic brachytherapy has been used as treatment for both benign and malignant tumors. Sources that were used in the past: high-energy, low-dose rate cobalt-60, low-energy X-rays, low-dose rate iodine-125, and

palladium-103, beta radiation-emitting low-dose rate ruthenium-106, and HDR strontium-90/yttrium-90. The source that's being evaluated by this subcommittee is Liberty Vision LV HDR beta-emitting radiation Y-90 disc.

Next slide, please? Y-90 has been widely used for cancer treatment, provided an effective treatment for episcleral fibrovascular growth. The treatment is to be provided by a team. That's the authorized user who is a radiation oncologist, the ophthalmologist, and the authorized medical physicist. The device with the LV Y-90 source was cleared by the FDA with a 510(k) with source activity up to 20 millicuries at time of treatment and 80 millicuries at time of shipment. And that's just because of the short half-life of the isotope.

Source can be used for either superficial lesions or at desired depth. And when we talk about depth, we're talking about a few millimeters.

Next slide, please? And again, the short half-life is 64 hours. That's a little over two-and-a-half days. The LV Y-90 source is designed for single use and to be stored for decay or return to the manufacturer. The desired dose prescription at specific depth is about 26 Gray, but that varies based

on the diagnosis.

Next slide, please? No, you're not looking at the eclipse here. You are looking at --

(Laughter.)

MEMBER OUHIB: -- the Liberty Vision source. And as you could see, this is the -- I'm not sure if you see the cursor that I'm using, but each source has its sole own serial number basically. And I'll come back to that later on why this is important.

The source is about six-millimeter diameter, so that's in this direction versus or that direction. And it's fairly thin. It's about one millimeter in thickness. And that's what they call a height basically.

Next slide, please? Okay. So, what you see at the top left there is the iWand A; that stands for anterior applicator, and its module. It's a very lightweight, 8 milligram. That's a good reason for that because the ophthalmologist will be using that to place actually the source where it needs to be. The middle left in here -- you see an anterior applicator with an imbedded Y-90 source, or disc I should say, placed to treat an underlying uveal melanoma.

The bottom left here; this is the iWand

P. That stands for posterior. And that applicator is designed for treatment of tumors and growths in the posterior aspect of the eye globe. And on the right-hand side here you see a graphical illustration. Shows the site defining tissue marking used to guide the placement of the iWand A on target.

Next slide, please? Okay. So, the treatment process, sort of the short brief diagram. Obviously, we have the written directives first and then the sources ordered. The source comes into the facility. It's calibrated and sterilized. That's just for the disc basically. And after that basically in the treatment room the iWand applicator is brought in and the source is actually sort of glued into the applicator. They use -- from I understood from the manufacturer right now they use Dermabond to actually make sure the source is in that little well of the applicator. It's a surgical skin glue-type of thing.

So once that's done it's put in a shielded area, that water pitcher shield basically. And once it's done and the ophthalmologist is ready, he will apply that to the patient. Treatment is performed. Time is recorded and so on. And then the applicator is removed and put in a pitcher shield and which -- eventually put in a disposal container,

which is a lead container. And that will be taken into radiation oncology. There's what it's kept either for decay or shipped to the manufacturer.

Next slide, please? Here's a treatment illustration with a case of microinvasive ocular surface malignant squamous carcinoma. And you could see that nodule right there basically and here's an enlargement of that. And to the right of that with the ultrasound you could see that elevated nodule there. This is after treatment. You could see a major improvement between the two and then you could also see it on the ultrasound. This is a one-month follow-up after HDL Y-90 plaque therapy.

Next slide, please? Patient and tumor characteristics without margin. This is important because of a geometric miss basically. So, you could see the location here. These are the ages of the patient. The thickness, 0.6 up to 1.7 millimeter. So probably this will be considered as superficial. The 0.6 and the 1.7 will be perhaps at depth. The width varies, basically a maximum of 4.1 and the length is about -- maximum of about 3.1. This is the staging for these lesions.

Next slide, please? Treatment parameters. These are the patient numbers basically,

but this -- you could look at the activity, the Y-90 source activity. These are in millicuries. The depth of treatment here. And here is the dose that was actually chosen for these lesions. And the duration here is in seconds.

Next slide, please? Central axis dose falloff. Why is this important? And that is when treating at a certain depth the AU could be aware of what is being delivered at the surface. So, if you're really delivering 100 percent here, 2.6 for instance, you can imagine what the dose is. That's six times the dose at 2.6, roughly speaking.

Next slide, please? The Brachytherapy Team and their role. The ophthalmologist is in charge of the diagnosis, the imaging part, target definition, and the applicator placement.

The AU is to provide the written directives, will assist on the applicator placement -- and that's their expertise basically because doing some of the brachytherapy we want to make sure that there is no geometric miss or anything like that -- the dose delivery, treatment planning, and radiation safety component.

The authorized medical physicist will determine the source activity and place the order, he

will calibrate the source, determine the time of the treatment planning, although the treatment planning is not quite available yet -- there's no manufacturer that provides that -- does the source sterilization, of course in charge of the radiation safety, and eventually the source disposal.

Next slide, please? Okay. So here are some specific recommendations by the Subcommittee. We felt like in Section 52 the Subcommittee recommends stating clearly the two different training pathways depending on whether the treatment is prescribed for the surface or prescribed at depth. For Section 522, should clearly describe that there are different training requirement for AUs treating superficial lesions versus AUs treating at depth. And Section 522(d), the Subcommittee strongly disagree with requiring a written attestation statement for involved non-AUs; i.e., an ophthalmologist for instance. Non-AUs are supervised individual and do not require preceptor attestation.

The Section 523, the Subcommittee recommends that this procedure be performed in the presence of an AMP. That's the authorized medical physicist. And the use of ophthalmic physicist should be deleted. There was no need for that.

Next slide, please? In Section 61, the Subcommittee recommends requiring the presence of both the AU and the authorized medical physicist. This is quite similar to other procedures such as intravascular brachytherapy, prostate brachytherapy, and other procedures where the AU and AMP are present during the procedure.

In Section 64, per the manufacturer's recommendation and other AAPM -- that's the American Association of Medical Physicists -- report calibration of the LV source must be performed by the user prior to use and compared to the manufacturer's stated activity. This is an important item for patient safety and accurate treatment. Any discrepancies must be resolved according to the AAPM Guideline, and that's to be within plus or minus five percent.

And why is that? I'll just give you an example here, a scenario that could potentially happen, hopefully never. A source of activity of 8.6 millicuries is ordered to deliver a dose of 25 Gray in 644 seconds. Let's just assume that the source received was not 8.76 millicuries but 60 millicuries. And if not checked for calibration and used for the same treatment time, it will deliver approximately

45.7 Grays versus 25 Gray. And that's about 82 percent more dose.

Let me clarify one more thing is that granted the user will receive a source certificate that will state what the activity is, the leak, and all that stuff. So yes, there is some other information for the user to look at. But it could very well happen where people think that they received the proper activity and proceed for treatment and next thing you know we have a medical event that was reported.

Next slide, please? Section 65, service and maintenance is not needed as this is a single-use device. Recommend deleting this section.

Section 66, the Subcommittee recommends replacing return to the safe shielded position with return to the shielded container that's provided by the manufacturer.

Next slide, please? The Subcommittee recommends that the LV Disc and iWand System present a few challenges, and that's accounting for anisotropy of the source when performing the treatment plan and that basically this is -- if you want to think about it, looking at the disc it's sort of like a dome when it comes to dose distribution.

So, toward the center you have more radiation coming in versus at the edges where you will have less dose coverage.

Properly positioning and orienting the iWand. And that is when I was talking about using a surgical thin glue-type of thing to mount the disc on the iWand. That was a concern, and we think that the users should follow direction from the manufacturer carefully. And that's the next item that I just talked about; number C. Members of the treatment team should take precautions to assure that they're of the source is in accordance with the manufacturer instructions.

Next slide, please? This is the list of our acronym, and I think that ends my presentation. I'm open to any questions. Thank you.

CHAIR JADVAR: Thank you, Ouhib.

We have a question. Melissa Martin?

MS. MARTIN: Hi, this is Melissa Martin. Hi, Zoubir.

MEMBER OUHIB: Hi.

MS. MARTIN: When you say calibrate, the first -- basically one of the first things you have to do is calibrate the source when you get it into your department. What are you recommending or what

is to be used to perform that calibration? Is it a dose calibrator? Is it a survey meter? Is a dosimeter? In other words, what do you actually use to calibrate that source?

MEMBER OUHIB: Thank you, Melissa. That's a great question. I asked the manufacturer regarding that, and it appears according to some colleagues -- because I called one ADCL basically to look into this. And as it stands right now there's really no per se a calibration designed for this source yet. The way they did it, it was a little bit very complex. They did a Monte Carlo also. But it's not quite straightforward. But my understanding is that there is one graduate school who is actually looking at this to make sure that this can be calibrated, maybe with a well chamber, maybe with a survey meter. It's left to be seen.

CHAIR JADVAR: Any other questions?

But, Melissa, you're still --

MS. MARTIN: No, there's just --

CHAIR JADVAR: Go ahead.

MS. MARTIN: -- there's nothing that's cited. There's certainly no commercial system to do this.

MEMBER OUHIB: That's correct. Yes.

That was one of my big concerns because people felt like, oh, well, you could use the manufacturer's source activity, but I feel very strongly that a calibration has to be performed to confirm that you are receiving what you ordered.

CHAIR JADVAR: -- then Dr. Harvey?

MEMBER FOLKERT: So, Michael Folkert. I do think that they're looking at with the radiochromic film. I think that was one of the ways that they were going to check and see what the dose distribution is across the disc.

MEMBER OUHIB: Yes, and that's only one way to do that, absolutely. Yes.

CHAIR JADVAR: Okay. All right. Dr. Harvey?

MEMBER HARVEY: Hi, Richard Harvey. Just a basic question. So, would this just be indicative for lesions on the front of the eye, or could it be used anywhere?

MEMBER OUHIB: It could be anywhere within the outside the eye. It could be on the front -- on the anterior, could be posterior, whatnot. So, but it also is accessible. So, if the ophthalmologist feels like he can place the applicator in a safe way and deliver the dose that's intended, then why not?

MEMBER HARVEY: Richard Harvey again. So, like we do ophthalmic brachytherapy now, would they go to the OR and take the eyeball out and irradiate the back of the eye and put it back in in one surgery so we could avoid the two surgeries the way we do it now?

MEMBER OUHIB: I'm not clear about the process itself so I can't say anything to that. I really don't. And that was not part of our charge.

CHAIR JADVAR: I'm just wondering actually -- from the clinical point of view I wonder if you can comment on how many times this has to be done when they order one and they put one over some lesion, for example one of the examples you showed. Let's say it's superficial and you don't have to go behind the eye, what is the efficacy? Do they have to redo this again once in a while or how effective is this?

MEMBER OUHIB: My understanding, this is a one-time treatment per se. So, let's just say that there is a recurrence there. I'm not really sure how they're going to proceed with that and use some sort of a BDE or whatnot to determine whether the second treatment is appropriate or not in terms of dose because now you're delivering a dose to the surface

and if you're going to retreat that lesion, what is that going to do to that area? I don't know.

CHAIR JADVAR: Any other comments by the Subcommittee members or Committee members?

Dr. Folkert?

MEMBER FOLKERT: I mean just for -- Michael Folkert. Just for additional information. It's all meant to be single fraction treatments. So, the superficial lesions are either benign or conjunctival melanoma or squamous cell carcinomas, the at-depth ones are more of the ones that are interior to the surface of the eye. So those are kind of the more traditional ones treated with plaque brachytherapy, but it's all meant to be single fraction treatment.

And if they're treating anteriorly, it would just be placed directly on the surface. If they're treating posteriorly, they usually do like a block where they paralyze the eye and then they move it physically to the side and place that curved applicator around it from behind, but they don't have to usually remove -- they don't have to unseat the eye in order to do that.

MEMBER OUHIB: Right.

MEMBER FOLKERT: Generally, they're not

supposed to --

MEMBER HARVEY: One surgery instead of two.

MEMBER FOLKERT: Just one surgery, yes. It's not meant to be removing any of the ocular muscles or anything.

CHAIR JADVAR: Okay. Thank you.

Any other comments or questions? Melissa?

MS. MARTIN: So just to clarify or follow up on a point that I asked earlier. So, from the manufacturer when you get one of these discs it actually gives you an activity and a dose rate on the certificate and that's how you would use that to calibrate -- calculate your time of treatment?

MEMBER OUHIB: That is correct, yes.

MS. MARTIN: Okay.

CHAIR JADVAR: Okay. Any other comments by the Committee members?

(No audible response.)

CHAIR JADVAR: Okay. Any comments or questions from NRC staff?

DR. VALENTIN-RODRIGUEZ: I only had one comment. And to Zoubir's point we do allow under our regulations in Part 35, specifically 35.432(b), for

licensees to use measurements by the source manufacturer to comply with the requirement that they need to do a calibration measurement before first medical use. So that is allowed by our regulations.

CHAIR JADVAR: Thank you. Any other comments by the NRC staff? Richard?

MEMBER HARVEY: I don't know the answer to this question which is why I'm asking it. Is it exempt it from a sealed source inventory or a leak test because of its transient nature or its short half-life? I mean, other sources are all leak tested and inventoried, so does this one got an out?

DR. VALENTIN-RODRIGUEZ: Maryann, I don't know -- I believe they have an SS&D, but I'm not sure.

MEMBER OUHIB: Yes, and they provide you with their own leak test basically, so you have it in your certificate that the source has been tested for that.

MS. AYOADE: Okay. Maryann Ayoade with the NRC. I do not believe that they are exempt from the leak test. It's a temporary one-time use source. Typically, what they can do is use it one time once it's attached to the applicator and they're either storing it for decay in storage or sending it directly to the manufacturer.

CHAIR JADVAR: Okay. Dr. Harvey?

MEMBER HARVEY: Yes, Richard Harvey. So, I don't think we're leak testing these sources when they come in.

MS. AYOADE: It's going to be handled the same way we handle the regular manual brachytherapy sources or any other sources that they have under 35.400.

MEMBER HARVEY: I don't think we're leak testing those currently because they're only transiently used and they're only at the facility for a very short period of time before they're sent back.

MS. AYOADE: But whatever the --

MEMBER OUHIB: But they're not being sent back. They're not. Well, I apologize. I take it back. So --

MEMBER HARVEY: They might be.

MEMBER OUHIB: -- I think as a user -- yes, that's correct -- as a user if I'm getting a radioactive -- whether it's the disc or a seed or whatnot, I will always test for leakage because you don't know what has happened coming in from the facility to my facility. Granted I have a leak test certificate from them, but I want to confirm that nothing has happened to that source. And why not do

a leak test on that and confirm that you are using an intact source that's not leaking basically.

MEMBER HARVEY: Richard Harvey. I'm just going to verify back at our place whether our therapy physicists are doing a leak test. Maybe they are and I'm not aware of it, but I wasn't aware that they were. They might very well be though. Thank you.

MEMBER AYOADE: So, Katie just referenced, and she just confirmed in 35.67 that they don't need to leak test because of the shorter half-life for these. And that's 35.67.

DR. TAPP: And their seal source and device registration also say they're leak tested prior to distribution.

MEMBER OUHIB: Yes.

DR. TAPP: There would be a certificate for leak testing in the initial ship.

MEMBER OUHIB: I'm just concerned that if something happened to the source itself while being shipped on its way to the facility. You never know. An accident or whatnot, or just bounced a little bit harder than it needs to be. I don't know that. Would that cause any -- I guess the manufacturer could probably answer that better.

CHAIR JADVAR: Richard Green.

MEMBER GREEN: Yes, should we recommend to the Subcommittee that they recommend that this licensing guidance provide instructions for Agreement State licensees -- Agreement States as well as licensees about these issues we're discussing now about leak testing and -- I mean, maybe I don't leak test it. I have one that comes with it. Maybe I assume it's good and it's intact for use, one-time use. Then it's decay and storage, but I still need to keep my records until it's either decayed in storage an gone or returned back to the manufacturer. But I'm sure likely questions are going to come up either from licensee or from the Agreement States.

MEMBER OUHIB: That's a good point.

MEMBER SHOBER: So, this is Megan Shober. With the 64-hour half-life the leak testing isn't a regulatory concern, and that's very clear in the regulations. So, I wouldn't foresee questions from Agreement States about leak testing for this product.

CHAIR JADVAR: Thank you. Any other comments?

(No audible response.)

CHAIR JADVAR: In the interest of time, I'm just going to move on with regard to have a motion for accepting the Subcommittee report.

MEMBER HARVEY: I'll make the motion to accept the Subcommittee report.

CHAIR JADVAR: Thank you. All in favor, say aye?

(Chorus of aye.)

CHAIR JADVAR: Any opposed?

(No audible response.)

CHAIR JADVAR: Any abstention?

(No audible response.)

CHAIR JADVAR: The report is accepted and the motion carries. Thank you.

So, it's 4:00. We're going to move onto our next agenda item, Item No. 11. It is ACMUI Reporting Structure and Ms. Armstead is going to present.

MS. ARMSTEAD: Lillian Armstead. I will be providing the review of the reporting structure. This presentation will go over the current reporting structure, a discussion of our annual review, the frequency of our meeting, and we'll have a discussion by the ACMUI.

This slide provides a graphic of the current reporting structure. Working up from the bottom the ACMUI reports directly to Mr. Kevin Williams, who is the Director of the Division of

Materials Safety, Security, State, and Tribal Programs, also known as MSST. Reporting to Kevin is Christian Einberg, who is the Branch Chief for the Medical Safety and Events Assessment Branch, known as MSEB. And our division MSST reports to Mr. John Lubinski in the Office of Nuclear Materials Safety and Safeguards. And it goes up the chain to our Acting Executive Director of Operations Raymond Furstenau, who reports to the Commission.

The ACMUI does not report directly to MSEB, however within this branch resides the Medical Radiation Safety Team which helps to support the day-to-day activities of the committee.

During the presentation of the bylaws of 2012 the ACMUI recommended to have an annual review of its reporting structure. At that time the ACMUI was presented with the option to continue to report to NMSS or to report directly to the Commission. The Subcommittee report provided in 2012 stated that the working relationship between the NRC and the ACMUI remained excellent and the reporting structure through the NRC staff continued to function effectively.

The Subcommittee and ACMUI agreed at that time that the associated logistics with directing

report to the Commission such as more frequent meetings did not and does not justify any change in the ACMUI's reporting structure.

The ACMUI currently holds two meetings each year: one in the spring, typically March-April, and one in the fall, typically September-October. The ACMUI also meets via teleconference approximately two to three times between these meetings and on an as-needed basis.

At this time, I'll turn it over to Dr. Jadvar and the ACMUI for discussion on whether the Committee is satisfied with the current reporting structure, what's working and recommendations on how to improve.

Dr. Jadvar?

CHAIR JADVAR: Thank you, Lillian.

So, you heard the question. Are you satisfied with the reporting structure that was just presented to us or do you think it can be improved in some way? Any questions/comments on that basis?

Dr. Harvey?

MEMBER HARVEY: I'm very satisfied. Thank you.

CHAIR JADVAR: Any other comments?

(No audible response.)

CHAIR JADVAR: Looks like everybody's pretty satisfied with the current structure. Thank you so much for that presentation.

All right. Moving onto Item No. 12, which is open forum. And I think Dr. Celimar Rodriguez is going to present some material on that.

DR. VALENTIN-RODRIGUEZ: Thank you, Dr. Jadvar. This is Celimar. I don't know if you all had any items you wanted to discuss now, but I have a few subcommittees here that I'd like to take -- to present to the ACMUI to either reestablish or establish new subcommittees to look at three items.

The first one is the ACMUI Bylaws Subcommittee. The NRC staff believes that it would be in the best interest of the ACMUI to take a look at their bylaws and update them, specifically regarding the conflicts of interest section to expand on what the responsibilities of each member should be with regards to any potential conflicts of interest.

We'd be interested in the Committee to do a report sometime in the fall of this year and we propose the following members: Dr. Wolkov as chair, Rebecca Allen, Michael O'Hara, and Richard Green.

Any questions or any comments on that?

CHAIR JADVAR: Thank you. I think that's

a very useful subcommittee and charge. And so, we have Dr. Wolkov is going to be the chair?

DR. VALENTIN-RODRIGUEZ: Well, that our proposal, but --

CHAIR JADVAR: That's your proposal?

DR. VALENTIN-RODRIGUEZ: -- open to --

CHAIR JADVAR: Dr. Wolkov, do you accept?

(No audible response.)

CHAIR JADVAR: Thank you so much.

And Ms. Allen who's not here today, and Dr. O'Hara, and Richard Green, right?

(No audible response.)

CHAIR JADVAR: All right. I think that's quite good.

DR. VALENTIN-RODRIGUEZ: Okay.

CHAIR JADVAR: Thank you.

DR. VALENTIN-RODRIGUEZ: Thank you. The next subcommittee. This would be a new subcommittee. Back in the fall of last year you all received a presentation from NRC staff regarding an effort to update the regulations in 10 CFR 30.35 that deal with financial assurance for Category 1 and Category 2 material. The staff is ready to provide that draft proposed rule to the ACMUI for review considering that there are certain Category 1 and 2 sources that

are used by medical licensees.

So therefore, the NRC staff is requesting that the ACMUI review and comment on that proposed rule. And that would be for a teleconference within 90 days, so we're looking at probably late-summer 2024. Our recommendations for a subcommittee include Mr. Richard Green as chair, Dr. Richard Harvey, Dr. Harvey Wolkov, and Mr. Zoubir Ouhib.

CHAIR JADVAR: All right. You heard. So, we are charged to review this proposal and comment on it with a teleconference sometime in this summer.

Mr. Green, you accept to be the chair?

MEMBER GREEN: I do.

CHAIR JADVAR: Okay. Thank you.

And then we have Dr. Harvey, Dr. Wolkov, and Zoubir Ouhib to participate. I hope everybody's agreed to that.

MEMBER HARVEY: Pleasure to.

CHAIR JADVAR: Okay. Thank you so much.

Very good. Thank you, Celimar.

DR. VALENTIN-RODRIGUEZ: Thank you. And the last subcommittee would be the reestablishment of the Interventional Radiologists Subcommittee. In its final report the ACMUI looked into whether it needed to update its membership to include an interventional

radiologist representative. And at that time because an update to the membership would require a document or a policy paper to the Commission, the ACMUI recommended to include an interventional radiologist as a non-voting medical consultant to the ACMUI for a trial period and to reassess at that time.

So therefore, consistent with the ACMUI recommendations we're asking that the ACMUI reassess whether they'd like to propose to the Commission a change in the membership of the ACMUI to include an interventional radiologist.

So, for this subcommittee we are proposed Dr. Einstein as chair, Dr. Jadvar as a member, Dr. Folkert, and Ms. Rebecca Allen. I'm open to any other suggestions, Dr. Jadvar, if you want to add a fifth member.

CHAIR JADVAR: All right. Great. Well, I personally believe that participation of Dr. Angle has been extremely useful and helpful to all of us. Thank you for your service.

And I'll be happy to participate in this subcommittee. And Dr. Einstein is not here, but I'm sure -- I'm not sure, but I feel that he will agree to chairing this. And we have Ms. Allen and Dr. Folkert. Is there anybody else who want to

participate?

MEMBER HARVEY: Richard Harvey. I'd be open to it if needed.

CHAIR JADVAR: Okay. Thank you so much. Thank you, Celimar.

DR. VALENTIN-RODRIGUEZ: Thank you, Dr. Jadvar. And that's it. That was more than enough for me.

CHAIR JADVAR: All right. But this is open forum, so just like this morning if there's anything that comes to your mind you want to discuss, this is the time to do it, please.

(No audible response.)

CHAIR JADVAR: No items?

(No audible response.)

CHAIR JADVAR: Okay. Very good. So, we are moving onto the last item on the agenda for today, administrative closing. This is also given by Ms. Lillian Armstead.

MS. ARMSTEAD: So, this year for the fall conference we're looking at the months of September, October, and November. The dates you select will be provided to the staff and the Office of the Secretary and hopefully they will be able to align with one of your proposed dates for the meeting.

Here are the dates: For the month of September, we have -- tentative dates are the 9th and the 10th. And as you can see, they're surrounding national meetings and holidays. For the month of October, we have tentative dates for the 7th and the 8th. And again, there is a list of holidays and meetings. And for the month of November, we have tentative dates for the 4th and the 4th. And also, national meetings and holiday.

So, at this time can the ACMUI make a selection?

CHAIR JADVAR: All right. Did we already vote on any of these? Do you have anything on that?

MS. ARMSTEAD: Yes, the most popular date was the November timeline.

CHAIR JADVAR: Okay. September is the certain not good for me, so that -- I know that. But I'm personally open to October or November.

And anybody else want to comment what their preferences are?

MEMBER HARVEY: Richard Harvey. I would prefer October, but I will certainly participate whenever it's decided.

CHAIR JADVAR: Anybody else? Dr. Folkert?

MEMBER FOLKERT: I would prefer November, but October also works. September would be very difficult.

CHAIR JADVAR: Yes. Anybody else on this side?

(No audible response.)

CHAIR JADVAR: All right. So --

DR. FAIR: Hi, it's Joanna. Sorry. I just want to say for --

CHAIR JADVAR: Hi, Joanna.

DR. FAIR: -- hi -- that week is Balloon Fiesta in Albuquerque and so traveling in and out of Albuquerque is very difficult. So that's my only preference for not October. It's just really hard to get here and there.

CHAIR JADVAR: So, you prefer November?

DR. FAIR: That's correct.

CHAIR JADVAR: Okay. And Zoubir? Are you on still?

MEMBER OUHIB: Yes, I am.

CHAIR JADVAR: Zoubir?

MEMBER OUHIB: Yes, I am.

CHAIR JADVAR: Okay. What is your preference?

MEMBER OUHIB: It's whatever work for

everybody. October or November will be fine. Thank you.

CHAIR JADVAR: Okay. So, should we consider November then?

DR. ANGLE: I have a conflict that date, but -- November. Sorry. Dr. Angle speaking.

CHAIR JADVAR: Joanna, you're not able at all to come in October?

DR. FAIR: I can. It is that the air travel is very challenging during that time to and from Albuquerque, but it -- will make it work.

CHAIR JADVAR: Okay. Is it because you are following --

DR. FAIR: Everybody in the United States is there during that time.

(Laughter.)

CHAIR JADVAR: All right. So, seems to me October may be good for almost everybody, right? Except Joanna will have some challenge.

You said October is no good?

And, John, you're okay October?

DR. ANGLE: I can make October work. Thank you.

CHAIR JADVAR: Okay. All right. I think you have -- with the compromise October is good?

Yes, Dr. Harvey?

MEMBER HARVEY: Richard Harvey. I'd make the motion for the October dates for the next fall meeting.

CHAIR JADVAR: Okay. Any seconds?

PARTICIPANT: I second.

CHAIR JADVAR: All in favor, say aye?

(Chorus of aye.)

CHAIR JADVAR: Any opposed?

(No audible response.)

CHAIR JADVAR: Any abstention?

(No audible response.)

CHAIR JADVAR: All right. So, let's have our meeting for the fall in the October dates, which was I think 7 and 8. Monday, Tuesday.

MS. ARMSTEAD: That's correct, Dr. Jadvar.

CHAIR JADVAR: Yes. Thank you.

Is there anymore of the administrative closing items?

MS. ARMSTEAD: That's it.

CHAIR JADVAR: That's it?

MS. ARMSTEAD: Yes.

CHAIR JADVAR: All right. So that's actually at the end of our agenda and we are done for

the day's activity. The meeting is adjourned. Thank you so much, everyone, for participating.

(Whereupon the above-entitled matter went off the record at 4:13 p.m.)