Official Transcript of Proceedings

NUCLEAR REGULATORY COMMISSION

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

Docket Number: (n/a)

Location: Teleconference

Date: Monday, September 21, 2020

Work Order No.: NRC-1059 Pages 1-153

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NUCLEAR REGULATORY COMMISSION

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ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

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TELECONFERENCE

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MONDAY,

SEPTEMBER 21, 2020

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The meeting was convened via Teleconference, at 10:00 a.m. EDT, Darlene F. Metter, M.D., ACMUI Chairman, presiding.

MEMBERS PRESENT:

DARLENE F. METTER, M.D., Chairman

A. ROBERT SCHLEIPMAN, Ph.D., Vice Chairman

GARY BLOOM, Member

VASKEN DILSIZIAN, M.D., Member

RONALD D. ENNIS, M.D., Member

RICHARD L. GREEN, Member

HOSSEIN JADVAR, Member

MELISSA C. MARTIN, Member

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

ZOUBIR OUHIB, Member

MICHAEL SHEETZ, Member

MEGAN L. SHOBER, Member

HARVEY B. WOLKOV, M.D., Member

NRC STAFF PRESENT:

KEVIN WILLIAMS, Director, NMSS/MSST

JACOB ZIMMERMAN, Acting Deputy Director, NMSS/MSST

CHRIS EINBERG, NMSS/MSST/MSEB, Designated Federal Officer

MARYANN AYOADE, NMSS/MSST/MSEB

STEPHANIE BUSH-GODDARD, RES/DSA

THERESA CLARK, NMSS/REFS

SAID DAIBES, Ph.D., NMSS/MSST/MSEB

DANIEL DIMARCO, NMSS/MSST/MSEB

LISA DIMMICK, Team Leader, NMSS/MSST/MSEB

JASON DRAPER, R-III/DNMS/MIB

ROBIN ELLIOTT, R-I/DNMS/MLAB

ROBERT GALLAGHAR, R-I/DNMS/MLAB

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VALERIE GRAY, NMSS/MSST/MSEB

MICHELLE HAMMOND, R-IV/

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IAN IRVIN, OGC/GCLR/RMR

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PENNY LANZISERA, R-I/DNMS/MLAB

SARAH LOPAS, NMSS/MSST/MSEB

KATHY MODES, NMSS/MSST/SLPB

ROBERT ORLIKOWSKI, R-III/DNMS/MLB

VERED SHAFFER, RES/DSA/RPB

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MELONIE WISSING, VA Ann Arbor Healthcare System

JOHN WITKOWSKI, UPPI

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

Opening Remarks.....8

Old Business.....20

Open Forum.....27

Medical Events Subcommittee Report.....38

Non-Medical Events.....63

New Drug Development and Labeling.....94

Dosimetry Methodology Update for

Regulatory Guide 8.39.....108

P R O C E E D I N G S

10:06 a.m.

CHAIRMAN METTER: Thank you very much, and good morning and welcome to the 2020 fall ACMUI meeting. But before we start, I would like to thank the ACMUI Committee, the NRC staff, and our guests for their flexibility and support of this virtual platform, so that the ACMUI can continue its work for the health and public safety of our patients and the public. I would also like to acknowledge the foresight and the work of the NRC staff and the ACMUI Subcommittee in proposing and implementing recent regulatory relief efforts during the COVID-19 pandemic. Thank you.

So at this time, I'd like to introduce Mr. Chris Einberg, who will open the meeting, followed by Mr. Kevin Williams, who will provide opening remarks.

Mr. Einberg.

MR. EINBERG: Thank you, Dr. Metter, and good morning. As the Designated Federal Officer for this meeting, I am pleased to welcome you to this public meeting of the Advisory Committee of the Medical Uses 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.

Participating today we have Lisa Dimmick, our Medical Radiation Safety Team Leader, and Kellee Jamerson, our ACMUI Coordinator, as Designated Federal Officers for the ACMUI.

This is the announced meeting of the committee that is being held in accordance with the rules and regulations of the Federal Advisory Committee Act and the Nuclear Regulatory Commission. This meeting has been transcribed by the NRC, and then may also be transcribed or recorded by others. This meeting was announced in the July 28, 2020 edition of the Federal Register, Volume 85, page 45445.

The function of ACMUI is to advise staff on issues and questions that arise on the medical use of byproduct material. The Committee provides counsel for 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 discuss today, but I also recognize there may be

minority dissenting opinions. If you have such opinions, please allow to be read into the record.

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

Dr. Darlene Metter, ACMUI Chair, Diagnostic Radiologist.

CHAIRMAN METTER: Present.

MR. EINBERG: Robert Schleipman, ACMUI Vice Chair, healthcare administrator.

VICE CHAIR SCHLEIPMAN: Good morning, present.

MR. EINBERG: Gary Bloom, patients' rights advocate.

MEMBER BLOOM: Present, good morning.

MR. EINBERG: Dr. Vasken Dilsizian, nuclear cardiologist.

MEMBER DILSIZIAN: Present.

MR. EINBERG: Ron Ennis, radiation oncologist.

MEMBER ENNIS: I think you said Ron Ennis, here.

MR. EINBERG: Right, I did. Mr. Richard Green, nuclear pharmacist.

MEMBER GREEN: Present.

MR. EINBERG: Hossein Jadvar, nuclear

medicines physician.

MEMBER JADVAR: President -- I'm sorry, present.

MR. EINBERG: Very good. Ms. Melissa Martin, nuclear medicine physicist.

MEMBER MARTIN: Present.

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

MEMBER O'HARA: Present.

MR. EINBERG: Zoubir Ouhib, radiation therapy physicist.

MEMBER OUHIB: Present.

MR. EINBERG: Mr. Michael Sheetz, radiation safety officer.

MEMBER SHEETZ: Present.

MR. EINBERG: Megan Shober, state government representative.

MEMBER SHOBER: Present.

MR. EINBERG: And Dr. Harvey Wolkov, a radiation oncologist.

MEMBER WOLKOV: Present.

MR. EINBERG: All members participating, so we have a quorum. All members of the ACMUI are subject to the federal ethics laws and regulations and receive annual training on these requirements. If a

member believes that he or she may have a conflict of interest as that term is broadly used within 5 CFR Part 2635 with regard to an agenda item to be addressed by the ACMUI, this member should divulge it to the Chair and the 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 in which they may have conflict of interest unless they receive a waiver or prior authorization from the appropriate NRC official.

Due to the COVID-19 pandemic, the NRC is continuing to allow flexibility in telework status. As such, we are all working remotely and each individually calling in for this meeting. I now ask NRC staff who are participating by phone to identify themselves. So we'll start with the Medical Radiation Safety Team.

MS. DIMMICK: Lisa Dimmick.

MS. HOWE: Dr. Donna-Beth Howe.

MS. TAPP: Dr. Katie Tapp.

MS. LOPAS: Sarah Lopas.

MS. GRAY: Dr. Anita Gray.

MR. EINBERG: NRC headquarters staff members participating.

MR. WILLIAMS: Kevin Williams.

MR. IRVING: And Ian Irving with the Office of General Counsel.

MS. HOUSEMAN: And Esther Houseman with the Office of the General Counsel.

MR. EINBERG: Individuals participating. I'll start with Region I. Three? Four? They may be in listen-only mode, actually. Okay.

Let's see, members of the public who notified Ms. Jamerson that they would be participating on the teleconference or registered for the Webex will be captured in the transcript. Those of you who did not provide prior notification, please contact Ms. Jamerson at kellee.jamerson@NRC.gov., and Kellee is spelled K-E-L-L-E-E, dot Jamerson, J-A-M-E-R-S-O-N @ NRC.gov, at the conclusion of this meeting.

We are utilizing a bridge line for the audio of today's meeting, and that phone number is 888-396-8716. The participant passcode is 7985339. The meeting is also using the Webex application to view presentation material in real time. You can access this by going to USNRC.webex.com, USNRC.webex.com, and searching for event number 1997447681, event number 1997447681.

The meeting material and the agenda for

this meeting can also be accessed from the NRC's public meeting schedule. Dr. Metter, at her discretion, may entertain comments or questions from members of the public who are participating with us today.

Individuals who would like to ask a question or make a comment regarding a specific topic the Committee has discussed should dial star-one to signal the operator that you wish to speak. Please clearly state your first and last name for the record.

Comments and questions are typically addressed by the Committee at the end of a presentation after the Committee has fully discussed the topic. We will notify the operator when we are ready for the public comment period of the meeting.

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

I would also ask everyone to exercise extreme care to ensure that the background noise is kept at a minimum, as any stray background sounds could be very disruptive on a conference call this large.

I will now turn the meeting over to Mr. Kevin Williams, Director of the Division of Material Safety and Security at State and Tribal Programs, for some opening remarks. Thank you.

Kevin.

MR. WILLIAMS: Thank you, Chris. Good morning, everyone. As Chris stated, I am the Director of MSST. I would like to welcome everyone to the fall 2020 ACMUI meeting. I first want to begin by thanking the ACMUI for all your hard work and support to the NRC. We truly value your contributions, your knowledge, and your expertise.

With full recognition of the ongoing COVID-19 public health emergency and following directives to minimize face-to-face interactions, the NRC asked you to conduct this meeting of the ACMUI remotely using Webex, and we really appreciate your efforts to support.

The ACMUI meeting with the Commission, initially scheduled for March 31, has been rescheduled for November 18, 2020, and we look forward to the upcoming engagement. I would like to highlight a few items that may be of interest to the ACMUI, as well as any of the meeting attendees in relation to Commission activity.

During the spring meeting, we told you that on January 13 of 2020, the NRC staff submitted a notation vote to the Commission, providing a rulemaking plan to revise the training and experience, commonly referred to as T&E, requirement for use of unsealed byproduct materials in 10 CFR Part 35.

The Commission is still deliberating on this topic, and once we have Commission directions through a staff requirements memorandum, we'll take the appropriate action.

On July 27 of 2020, the Commission approved the staff's recommended Option One to develop and propose to the Commission a limited revision to the abnormal occurrence, or AO, criteria in the medical event and source security areas only. A working group was recently developed to draft a revision to the AO criteria, and they'll be working with ACMUI AO Subcommittee.

With regards to NRC activity, we're currently focused on the emerging medical technologies rulemaking. The staff is developing a rulemaking plan with assistance from a working group that includes representatives from the agreement states, NRC Region I, and NRC rulemaking staff.

The plan will discuss rulemaking options

that would codify licensing requirements for some or all of the 10 CFR Part 35.1000, emerging medical technologies, into existing or a new subpart of Part 35. The ACMUI will receive a courtesy copy of the rulemaking plan in October, and the staff expects to deliver the rulemaking plan to the Commission either late December or early January of 2021.

We are currently continuing our evaluation of extravasation. The ACMUI Subcommittee provided recommendations on extravasation and infiltration at the September 2019 ACMUI meeting. Currently, the NRC staff is conducting an independent evaluation, and we provided the staff's report to Congress on March 17 of 2020. The staff is expected to complete its evaluation in spring of 2021.

Phase II revisions to Regulatory Guide 8.39. The process for the Phase II revisions to Regulatory Guide 8.39, release of patients administered radioactive material, began in October of 2019. The Phase II revisions will update the dosimetric equations, methodologies, and tables used to calculate dose to members of the public from released patients. You will hear more about this today from Dr. Hamby.

Reporting nuclear medicine injection

extravasations as medical events petition for rulemaking. On May 18 of 2020, a petition for a rulemaking was submitted requesting that the NRC revise its regulations to require reporting nuclear medicine injection extravasations that exceeded 50 rem dose equivalent to tissues as medical events.

The petition is currently open for public comment. You will hear more about this tomorrow from Lisa Dimmick.

ACMUI meetings. Since the spring 2020 meeting, the ACMUI held a public teleconference on April 30 of 2020 to discuss the COVID-19 Subcommittee's recommendations for regulatory relief measures during the COVID-19 pandemic. The Subcommittee provided for consideration of several specific recommendations for a temporary exemption. Thank you to the Subcommittee for their efforts.

The NRC staff has issued a total of 54 temporary regulatory exemptions for material licensees, a few of which were medically related. And we continue to focus on public health and safety during the processing of these exemptions.

The NRC organizational changes. Christopher Hanson was sworn in on June 8 of 2020 as the fifth NRC Commissioner. He will serve the

remainder of a five-year term expiring June 30 of 2024.

Michael Layton, the Director of MSST, retired on August 31 of 2020. I was selected as the MSST Director and officially started approximately the same time as Michael retired. That gave me the opportunity to select a Deputy.

Theresa Clark will be the MSST Deputy Director, and she will begin her new role in the week of September 27, and she will be joining us at the start of the next session of this meeting, approximately 12:15. And I would request from Dr. Metter that we take an opportunity to introduce Theresa.

Jake Zimmerman, and he is on the public side so he can't be unmuted, has been the Acting MSST Director since July of 2020.

So meeting items of high interest. The following Subcommittee reports and presentations will be discussed today. Dr. Ennis will discuss the Subcommittee's review and analysis of the medical events on the fiscal year -- on fiscal years 2016 to 2019. Mr. Sheetz will discuss his review and analysis of non-medical events from fiscal year 2018 to 2019.

Mr. Frank Lutterodt of the US FDA Center

for Drug Evaluation and Research, will provide an overview of the FDA process for new drug development and labeling. Lastly, Dr. Hamby will discuss the revisions to the methodology used in Regulatory Guide 8.39, phase II.

And Frank, if I mispronounced your name, I apologize. And at this time, I will turn the meeting back to Dr. Metter.

CHAIRMAN METTER: Well, thank you, Mr. Einberg and Mr. Williams for your comments and for opening the meeting and providing some opening remarks and reviewing the agenda for the meeting.

Next on the business is Ms. Kellee Jamerson, who will review past ACMUI actions and recommendations and provide NRC responses.

Ms. Jamerson.

MS. JAMERSON: Good morning, Dr. Metter and ACMUI members. I will be presenting the old business.

So this, we'll start with our 2019 ACMUI recommendations and action items. And recently I sent ACMUI members a memorandum from the staff providing detailed information on how some of these items have been dispositioned.

So beginning with number 17, 2019, this

item is referring to the appropriateness of medical event reporting Subcommittee report and the recommendations provided from that report. We had a presentation covering the overview of NMED at the spring meeting. And it was discussed then that the recommendations from the Subcommittee report regarding (audio interference) was provided.

So the staff determined that the ACMUI's specific findings regarding NMED were generally outside the scope of NMED's intended function. And so for that particular recommendation, the staff recommended that this item be closed.

But there's a second part to one of the recommendations, and that's regarding coordination with the ACMUI to provide additional information to NMED users on best practices for writing NMED reports for medical events.

And this part of the recommendation was accepted by the staff, and the staff plans to share best practices for preparing NMED reports. So this particular portion of the recommendation will remain open, with an anticipated completed date of spring 2021, which is what you will find here. And it's listed status is open, targeted completion date for spring 2021.

For item 18, the ACMUI endorsed the evaluation of the Extravasation Subcommittee report. This item also, as Kevin mentioned, our internal staff evaluation is ongoing are we are targeting a completion date of spring 2021. So this item will remain open as well.

For item number 20, the ACMUI endorsed the Institutional Memory Subcommittee report as amended to include the recommendation of the complete list of ACMUI members be updated and added to the webpage.

As you recall, we discussed --partially some of this had been covered from the spring meeting, that the web page was updated to include the full listing of the historical membership of the ACMUI members. And this is also covered as part of the memorandum that was issued recently for the ACMUI members.

There's also a portion of this that references a guide for new members, which includes information that could not be updated as part of the brochure, the NUREG. So it's been placed into a more internal document for ACMUI members once they have joined the Committee. And we will be discussing that as part of our closed session tomorrow.

And so with this, the staff is

recommending that we close this item per the response memorandum dated September 14.

Moving to 2020, ACMUI recommendations and action items. The first item is Regulatory Guide 8.39, release of patients administered radioactive materials. The Phase I of revision to Regulatory Guide 8.39 was issued in April 2020. And the staff has fully or partially accepted the ACMUI's recommendations and specific comments, and each of those was outlined in the memorandum that was provided to you.

For this reason, we recommend that item number one, the 2020, be closed, per the memorandum dated September 14.

For item number two, Dr. Metter formed a subcommittee to review the impacts that COVID-19 could have or is having on the medical use community and determine its potential impact to help the NRC prepare for any regulatory impacts.

This item, the Subcommittee met, presented their recommendations for the regulatory release measures on April 30. And for this, the NRC recommends that this item be closed as well, per the memorandum dated September 14.

Item number three. Dr. Metter amended the

membership of the Training and Experience Requirements Subcommittee. This membership was amended on March 30 during the spring meeting, and the ACMUI subcommittee web page has been updated to reflect that. And so the staff recommends that this item be closed as well.

For item number four, the ACMUI endorsed the Patient Intervention Subcommittee report as presented and the recommendations provided therein. The staff is continuing to evaluate the Subcommittee's recommendations related to extravasations and medical event reporting and patient intervention. And so the staff recommends that this item remain open, and we have a target date of spring 2021.

For item number five, the ACMUI endorsed the Bylaws Subcommittee report as presented. From this report at the spring meeting, the Subcommittee proposed no changes to the existing bylaws regarding term limits for the ACMUI Chair and Vice Chair. And this currently remains at the discretion of the Director of the Office of Nuclear Materials Safety and Safeguards. But the NRC staff accepts this recommendation, and we recommend that this item be closed.

For item number six, Dr. Metter formed a subcommittee to review the abnormal occurrence

criteria. Currently we have received direction from the Commission, as Kevin indicated, and the Subcommittee was placed on hold during, until further notice, during the spring meeting, and they are, will receive some guidance from NRC staff in the very near future.

But because this item, with the formation of the Subcommittee and they will receive their information from the NRC staff for the Subcommittee. For this reason, the NRC staff recommends that this item be closed.

For item number seven, the ACMUI endorsed the Interventional Radiologists Subcommittee Report as presented. And currently the staff is considering inviting an interventional radiologist as a nonvoting member per the Subcommittee's recommendations. And staff is still working on this. And per the -- per the memorandum, the staff recommends that this item be closed.

For item number eight, the ACMUI tentatively scheduled its fall meeting for today and tomorrow, which we are meeting. So the staff recommends that this item be closed.

For item number nine, this goes back to the COVID-19 Subcommittee report. As provided during

their April 30 meeting, there were a number of recommendations that were provided from that report for temporary relief and exemptions for medical licensees.

And those recommendations, for details of how those recommendations were dispositioned provided in the memorandum dated September 14. And for this reason, the staff recommends that this item be closed.

And that concludes the listing of the ACMUI's recommendations and action items from 2019 and 2020. If you have any questions, if the ACMUI has any questions, Dr. Metter. This concludes the old business.

CHAIRMAN METTER: Thank you, Ms. Jamerson. Are there any questions from the ACMUI regarding the contents that were reviewed that we recommended and the NRC response? Okay, hearing none, let's go ahead and let's go on to the next item on the agenda.

MS. JAMERSON: I'm sorry, Dr. Metter?

CHAIRMAN METTER: Yes.

MS. JAMERSON: This is Kellee.

CHAIRMAN METTER: Yes.

MS. JAMERSON: Did we have a motion the staff recommended for the items that are denoted with an asterisk to close those items, is there a motion

from the -- from the Committee to close?

CHAIRMAN METTER: Yes, thank you, Ms. Jamerson. Do I have a motion on the -- from the ACMUI Committee to close the open items that were listed as recommended by Ms. Jamerson?

MEMBER WOLKOV: So moved.

CHAIRMAN METTER: And who was that?

MEMBER WOLKOV: This is Harvey Wolkov.

CHAIRMAN METTER: Thank you, Dr. Wolkov. Do I have a second, please?

MEMBER JADVAR: Dr. Jadvar, second.

CHAIRMAN METTER: Thank you, Dr. Jadvar. Do I have any discussion? All in favor of approving the old business that was just reviewed by Ms. Jamerson and recommendations to close the items that she suggested, all say aye.

(Chorus of ayes.)

CHAIRMAN METTER: Any abstentions or other comments? Okay, Ms. Jamerson, it looks like we have no other comments and that the ACMUI Committee approves the actions proposed by the NRC staff. Thank you.

MS. JAMERSON: Thank you very much, thank you.

CHAIRMAN METTER: Thank you. Now, the

next item on the agenda is an open forum. Now, is there anybody in the Committee or anyone would like to suggest any medical topics of interest for future discussion for our future meetings? Okay, thank you. Any items from the NRC staff?

MEMBER SHEETZ: This is Mike Sheetz.

CHAIRMAN METTER: Yes.

MEMBER SHEETZ: I have one item to bring. It's not really a future business, a meeting item, but I do think it's an issue that I wanted to bring forward for clarification. With the onset of the COVID-19 pandemic, most meetings and training sessions have been converted to a virtual computer-based format.

Currently, in the regulations, the initial and annual HDR and Gamma Knife emergency training required under 35 610(e) states, A licensee shall ensure that operators, authorized medical physicists, and authorized users participate in drills of the emergency procedures initially and at least annually.

And so the issue is the, quote unquote, participate in drills part implied that this would be required to be done in person. However, a case could be made for a drill to be conducted virtually with visual illumination. I think it's important for the

NRC to clarify what is expected under this requirement as to whether this may be provided virtually or needs to be done in person with hands on the device.

This clarification will help licensees ensure that they're following the regulations and avoid different interpretations of the regulation by inspectors in both NRC and agreement states. Thank you.

CHAIRMAN METTER: Thank you, Mr. Sheetz. Regarding that, Mr. Einberg, would it be, or Kellee, would it be appropriate for the COVID Subcommittee to review this?

MR. EINBERG: Thank you, Dr. Metter and Mr. Sheetz. Perhaps Lisa Dimmick, the Medical Radiation Safety Team Leader, can discuss whether this has been -- whether this issue had been evaluated previously, and then we'll discuss whether it would be appropriate for the COVID-19 Subcommittee to evaluate it further.

So Lisa, do you have any insights on this?

MS. DIMMICK: Hi, it's Lisa Dimmick. A few things to think about or that we could discuss. So with regard to the initial and annual training for emergency procedures on HDRs and Gamma Knife, we did evaluate the regulatory requirement and identified

that the requirement for the annual safety emergency procedure training would be one where NRC staff could review an exemption request for that regulation. And in that, identify that licensees could request a temporary exemption for that initial -- or for that annual training, not the initial, but for the annual training, you know, for an extension of maybe up to 90 days.

We've discussed quite a bit about the work experience or training and also things like drills where it is implied that it would be hands-on or in-person type training. And we haven't yet issued or provided temporary exemptions that we could expedite for licensees. We could consider an exemption for participation in things like drills probably case by case.

There might need to be a unique situation for that. But to evaluate it as we've done for our other -- for other regulatory requirements where we're, you know, could expedite an exemption request.

The thing that facilities might want to consider is while doing a lot of these annual training requirements, people may bring in everyone to do the training at once. But maybe there's other ways you can achieve that training to think about, such as, you

know, some aspects of that emergency procedure training could be done virtually.

But the things that really require the hands-on operation in a drill, it's, that very difficult to fulfill that requirement or achieve that same level of training virtually. So we haven't yet issued any -- an exemption whereby we would see participation, active participating, could be sufficed virtually.

So it's something that we could discuss after the meeting, after this ACMUI meeting. But right now, we haven't done that, we haven't issued an exemption to exempt participation in things like drills or emergency procedures.

CHAIRMAN METTER: Thank you, Lisa. Do you have any questions, Mr. Sheetz, or is that helpful?

MEMBER SHEETZ: So, this is Mike Sheetz. So if I understand Ms. Dimmick correctly that the current regulatory requirement would expect this annual emergency training -- that those who participate in drills would have to be in person with hands on the device. And that to do it virtually, it would require a specific license exemption. Is that correct?

MS. DIMMICK: Yes, that's correct. But

what I'm also trying to say is that there might be ways that you could still fulfill maybe not -- I think, not -- to give an example or illustrate, perhaps everyone could receive the review of the emergency procedures virtually, but perhaps then the same staff who are receiving the training on drills are also going to be on site to be physically present during procedures.

So there might be ways to achieve some hands-on aspects of that annual emergency drill training or participation in drills while they're on site for patient procedures.

Again, it's maybe not the way facilities have typically done their training where they bring everyone together and do all of the training at once together. But perhaps there could be aspects of the emergency procedures that could be done virtually. But then parts of the training where you're having the hands-on experience could be done in a different -- could be done in person, but not necessarily collectively as a group.

So I think facilities need to think about how else they can achieve the hands-on part of it that might be slightly different than what they did before but achieve hands-on. That's what I'm trying to say.

But it -- where we talk about participation in drills, that does imply, would imply hands-on or in-person experience.

CHAIRMAN METTER: Thank you.

MEMBER SHEETZ: This is Mike Sheetz. Thank you. You know, I'm not advocating one way or the other, I just wanted to make sure it was clear what the NRC expected with respect to this participate in drill so that licensees don't get confused and think, well, we can do this virtually and so they would do (audio interference) at this time. At least not completely. So, thank you very much.

CHAIRMAN METTER: Thank you, Mr. Sheetz, for your question and thank you, Lisa, for the explanation.

Do I have any other topics that might be of interest for future discussion?

MR. EINBERG: As Kevin pointed out, we will be engaging with the ACMUI on the abnormal occurrence and as we do our evaluations and also with extravasation. So, I think there's a lot coming down the pike, but there's nothing in addition to what we've already mentioned.

CHAIRMAN METTER: Oh, thank you. Okay.

MEMBER GREEN: Dr. Metter, this is Richard

Green.

CHAIRMAN METTER: Yes, Richard.

MEMBER GREEN: I was just made aware of, you know, there are two manufacturers that manufacture yttrium-90 or Y-90 spheres for microembolization of hepatic tumors. And one of the manufacturers has a new optional delivery device, delivery system.

I just think that we should keep our eyes out and see if this introduction of this new optional delivery systems results in a decrease in the events related to Y-90 infusions.

CHAIRMAN METTER: Okay. And when is that out?

MEMBER GREEN: It's out commercially now. It's named S-I-R-O-S, SIROS delivery system. I just think, you know, it's new, it's exciting, I don't know if it'll result in a better infusion, better procedure, or whether it'll have any effect at all.

CHAIRMAN METTER: Okay. Well, thank you for that information, and that should be captured under the Medical Events Subcommittee purview. But thank you very much for bringing that up and bringing it to our attention.

Any other new topics or topics that would suggest?

MEMBER OUHIB: This is Zoubir. Just a question for Mr. Green. Now, my understanding, when a device like that comes on the market, that it has to go through the FDA. Do we have any feedback from the FDA representative on that at all?

MEMBER O'HARA: This is Michael O'Hara. No, we don't. I don't have anything formal to say, but I will look into this issue.

CHAIRMAN METTER: Thank you, Dr. O'Hara. Any other comments? Thank you for bringing -- oh, go ahead, I'm sorry, go ahead, I think that's Vasken.

MEMBER DILSIZIAN: Yeah, Yeah, Vasken Dilsizian. Yeah, I just wanted to bring a topic heads up. One of the exciting parts of cardiac perfusion imaging is that there's a F-18 label perfusion tracer that's currently in Phase III clinical trials that may go through the FDA approval and CMS reimbursement process.

What's different about it is that the F-18 would allow patients to be assessed during exercise, treadmill, rather than pharmacologic stress with all the current radiotracers. The good news is that we can have one radiotracer to do for pharmacologic stress and treadmill exercises, F-18 having a longer half-life.

The aspect that would be relevant for the NRC is what would be the occupational exposure to the technologists and physicians and nurses who are in the exercise lab who will be injecting the radiotracer at peak exercise.

So I'm just not sure when this topic would be relevant for NRC to discuss, after the FDA approval process or before. I just want to bring up that there is excitement in a new radiotracer that would be updating the perfusion tracer that would have occupational impact on those who are near the patient and injecting F-18 label perfusion tracer.

CHAIRMAN METTER: Thank you. Do I have any response of the NRC, from the NRC staff on this?

MS. DIMMICK: Hi, it's Lisa Dimmick. So we'll, I'll take this as a takeaway to evaluate. Typically we like to be aware and in evaluating some of the new, emerging technologies so we're aware of their uses, how they're administered before they maybe have been cleared or approved by the FDA so that there aren't issues for licensees who want to begin using these more broadly than outside of clinical trials.

So I'll -- so the Medical Team will do some, we'll evaluate this new, emerging radionuclide for the things that Dr. Dilsizian mentioned.

MEMBER DILSIZIAN: Thank you, Lisa. Just, you know, it's the F-18 Flurpiridaz is the name, the name of the radiotracer.

MS. DIMMICK: Okay.

MEMBER DILSIZIAN: Flurpiridaz.

CHAIRMAN METTER: Thank you, Dr. Dilsizian for bringing that up. Do I have any other topics from the ACMUI Committee for future discussion or review?

MEMBER OUHIB: This is Zoubir. I think this item was brought up in the past. This is regarding SaberDerm (phonetic), which basically uses palladium-103 seeds as a patch for -- and there is an interest in doing some sort of a skin brachytherapy using these patches. This will be a temporary implant, call it, you know, four, five days or something in that nature. And basically the patient will be sort of released with that patch and then brought back and have the patch removed. So there are still a lot of details going on regarding that.

Let me just go ahead and disclose that our institution is actually interested in that, but we have not finalized anything at this point.

CHAIRMAN METTER: Okay, thank you. I think that would be under the new emerging radiopharmaceuticals.

MEMBER OUHIB: Probably, so yes, thank you.

CHAIRMAN METTER: So I think we'll be looking at that and keep a -- but thank you for bringing that up and making us aware of this --

MEMBER OUHIB: Sure.

CHAIRMAN METTER: New type of brachy -- it's an interesting actual mode of treatment.

Any other topics or issues that are coming up that would be of interest for the medical topics for the ACMUI to address?

Okay, let's move on to our next topic, which is Medical Event Subcommittee report.

Dr. Ennis will provide an analysis of the 2019 medical events.

Dr. Ennis.

MEMBER ENNIS: Thank you, Dr. Metter. Good morning, everyone, can you hear me okay?

CHAIRMAN METTER: Yes.

MEMBER ENNIS: Excellent, okay. Kellee, you'll advance the slides for me? Great, thank you very much.

Well, good morning, everyone, it's my honor to present the annual report of the Medical Events Subcommittee. Next slide, please. Our

subcommittee members include myself, Richard Green, Darlene Metter, Mike O'Hara, Michael Sheetz, Harvey Wolkov. I thank them all for their invaluable work on this report, and to Dr. Donna-Beth Howe for her input as well. Next slide, please.

So you may recall the Subcommittee has existed for some time, but we advanced this approach a few year back and took on to do a four-year review every two years.

So we did this for the first time in 2018, we do the prior four years so that we have a bigger and wider lens to be able to look for trends, given the small number of medical events that are generally recorded but looking at an annual report was felt to be a little too myopic. So we had this broader review which we did two years ago, and we are now doing this again now for the second time. Next slide.

So two years ago we reported on two themes that seemed to stand out as areas for future emphasis to help decrease medical events and that these themes applied to varying degrees across the various aspects of radionuclide therapies. And these themes are again affirmed today, but we also see a possibility of a new one emerging.

The first, as you may recall, is the value

of performing a timeout immediately prior to administration of radioactive byproduct material. This is commonly done now, universally done, at least in this country for surgeries and in all kinds of other procedures.

And in our review, from the anecdotes of the medical events, it would seem that a decent proportion, and then we'll see the exact numbers as we go through, might have been or definitely would have been prevented or had the potential to be prevented, prevent a medical event.

The second thing is an apparent or implied lack of recent or frequent enough experience for a specific administration that may have been an important contributing factor. And again, this would lead to an encouragement of authorized users to review, do dry runs, things like that prior to doing a procedure that they are less familiar.

And one new issue that may be emerging is attributed to the increasing complexity of unsealed source administrations, some of the new agents. So this may be leading to more equipment-related medical events in that context. And you'll see some numbers later on.

And this will be something of course we'll

be looking for to see if this continues, and then obviously we might have some recommendations, some actions. At this point it's only just raising this as a potential issue for the future. Next slide, please.

So now going through each of the subsections. So for 35.200 on unsealed byproduct material for imaging and localization, as has been the case for years, really very low numbers of medical events in this context. Of the few events, though, a reasonable portion might have been prevented by the use of a timeout prior to administration. Next slide.

In 35.300, using byproduct material, unsealed byproduct material in which a written directive is required, some more events. No real trends in terms of increasing numbers per se, except for the one that I just alluded to before, equipment, where in 2019 there was a, you know, significant bump.

And reading through the actual events, it was a consideration that, you know, these may be all from the newer, more complex isotope deliveries. And this -- as these are expected, these isotopes and others like them, are expected to increase, we may be starting to see the emergence of another issue.

Again, not enough, certainly not enough cases and enough history to be established as a

definitive issue, but something that our subcommittee wanted to bring to the wider audience's attention.

Again, as in prior years, timeout seems to be able to be an important, potential very important issue in this particular area because a significant proportion of these medical events could have potentially been prevented by the use of a timeout. And yeah, thank you, next slide.

We go to manual brachytherapy. So the biggest change there is a better definition of a medical event when it comes to prostate brachytherapy, that as we, I think everyone here is familiar, rulemaking modified that. And that has gone into effect, and so we are now seeing fewer medical events, a good fewer medical events in that category. Appropriately, as the ACMUI and the NRC ultimately agreed, that the event, the definition was problematic.

Interestingly, though, there were still three medical events in this space, and all of them had still been using dose-based criteria. It was not clear if there would have been medical events if they had used radioactivity-based event. Aside from that, the number of events are low and no particular trends stand out in terms of numbers. Next slide.

Timeouts, again, could be helpful. And the lack of experience does continue in a few of the events to play a role. We've noted this before, about the same amount per year, but these issues do a seem to play a role in a decent proportion of the small number of events in this category. Next slide.

So, I think we've already summarized this. So, about 13% of cases, a timeout or enhanced retraining prior to performance for an uncommon procedure might have prevented medical events. So those two issues that we've highlighted throughout the last report and this contribute, potentially, to a small number, 13% or so, of the medical events.

I wouldn't really make much of slight changes in the proportions between the report from two years ago and now because the case numbers are relatively small; obviously, one case can make a difference in the percent, so I wouldn't really make anything of that specific change in number. Next slide.

Now, 35.600, sealed sources for remote afterloaders. Teletherapy units, Gamma Knife units that are licensed under 35.600. Again, similar numbers over the years, modest numbers. Nothing particularly alarming. Nothing disappearing, but

nothing increasing either. Next slide.

And just reviewing to what diseases these technologies are used. So, HDR therapy is the dominant one, and then other events are reported. HDR is used less these days in breast and lung. It's used in prostate a little bit more, but there does not seem to be an increasing number of medical events, which is positive. But we may see more if brachytherapy continues in prostate.

And obviously some of your Gamma Knife units are licensed under 35.600, so the (audio interference). Next slide.

And, again, timeouts could play a helpful role in limiting medical events. Estimates per year of how many events might have been helped by a timeout are given here. And, again, similar this year to the past year to the year before in proportions that are seen here, about 21% over this current four-year period might have been helped, might have been prevented if a timeout had been used. Next slide.

In terms of the infrequent user phenomena, if you will, smaller number of events seem to be an issue in this category. Potentially up to about 15% of events might have been prevented if users had done some interventions, like we alluded to before, prior

to doing an infrequently performed procedure. Next slide.

RSL, radioactive seed localization. Very few number of cases. But I don't have a good sense, to be honest, with how often this is being used. I think they are competing with other alternatives that have emerged since, but certainly it's being done safely overall. Next slide.

Turning to the intravenous cardiac brachytherapy, which is licensed 35.1000. Again, not a very commonly done procedure, but it has had a little bit of a re-emergence in the last years. And very few medical events as well. Difficult to really assess. Does not seem to be timeout issues. If there is a timeout done before these procedures. In general, it's done in hospitals (audio interference), all kinds of cardiac events there's always a timeout. All cardiac procedures a timeout done beforehand. Next slide.

Now getting to Gamma Knife, the Perfexion and Icon units. They're licensed under 35.1000. Very few events. It seems to be very safely done, as we've discussed in the ACMUI previously, and that seems to continue to be the case in 2019. Next slide.

Now we get to Theraspheres, Y-90

Theraspheres. And here, as we know, we have a significant number of events. No dramatic increase or decrease; about the same trends. We obviously don't have the denominator on exactly how many cases are being done. We've discussed that issue in the past as well. But everything, the trends -- there's no trends. Things are stable in this regard. Which, you know, obviously, it would be better if things were declining, but it could also be worse. So this is where we are. Next slide.

And same for SirSpheres. About the same number of cases per year and about the same problem as being the main one and the dominant one for both SirSpheres and Theraspheres are the leaving residual activity in the device. We have discussed the issues in the past. We are considering adding a nonvoting member to help with this topic a little bit, as well. Who knows, the previously alluded-to new delivery device, maybe this will help this problem. Obviously, that would be an excellent improvement if that were the case. So we'll have to look out for that. Next slide.

And just comparing the breakdowns and distribution of the types of events from the previous review from two years ago and this year's review. The

proportion of cases due to different events, different causes, is essentially the same, with more than 20% residual left in the device, (audio interference) almost two-thirds. Next slide.

So, preventing microsphere medical events. The action items would be for users to review the mechanics in the setup procedure beforehand, especially if they're unfamiliar with it. Some kind of timeout to confirm calculations and making sure the (audio interference). No changes in this area compared to prior years. Next slide.

And when it comes to all 35.1000 events, the timeout has an impact in the Gamma Knife space, the Perfexion Icon, and then the microspheres to some degree. Next slide.

And the infrequent user phenomena, again, may play a little role in the Gamma Knife, particularly; maybe a small role in the microspheres. Next slide.

And just as a suggestion, we've reviewed this before. This isn't really a change element, but could be considered in a timeout (audio interference) identity of the patient by two identifiers. In reviewing the exact procedures that will be performed, the isotope, the activity, and the dosage, a second

check on the calculation and making sure the written directive and dosage (audio interference). Next slide.

Other things that could be included depending on the application, the units of activity, different (audio interference) where we have seen some confusion between microcuries and millicuries. The anatomic location, the patient's name on the treatment plan matching the patient's name in the room, treatment plan, an independent check of the treatment plan. If the reference length has been checked correctly and determined to be (audio interference) correctly. It's always a recurrent theme that we have seen (audio interference) and that area and implant size are correct, which typically comes up in those few radioactive seed localization procedures. Next slide.

The Subcommittee recommended the NRC issue an information notice notifying authorized users to (audio interference) this with other Subcommittee recommendations from two years ago. And (audio interference) the NRC did do that, and this is a reference (audio interference) to the NRC's information that went out to the user community.

The Subcommittee wants to thank the NRC

for taking our recommendations seriously and acting on them, at least we all hope that it'll be read and will have an impact on the broader user community that you might be able to see over the next few years with the Subcommittee and user data. Next slide.

These are the acronyms included in the report. That concludes my report. Thank you for your attention, I'd be happy to take any questions.

CHAIRMAN METTER: Thank you, Dr. Ennis, for that very thorough report. And for implementing this new format, which is very informative.

And you know, even though the number of our medical events are small compared to the overall number of medical procedures using radioisotopes, I think this will assist our licensees in further decreasing the medical events if they comply or implement your recommendations. Thank you very much.

Do I have any questions from the subcommittee for Dr. Ennis?

MEMBER JADVAR: This is Dr. Hossein Jadvar. I have a question. So, this is interesting that you mentioned that 20 percent of the Y90 residual was not due to stasis.

Is it because it was, the 20 percent was not just delivered to the patient? And it just seems

to me that there is room for general, you know, room for general optimization of the set up and how this is being delivered to the patient.

And I wondered about this new delivery device or dose. Or what Richard Green just mentioned, if that's an attempt to induce this situation.

Can you kind of describe a little bit more of what you meant by 20 percent not at stasis?

MEMBER ENNIS: Right. So, in other words, it's considered a medical event. If it's due to stasis, it's not a medical event.

But, if that amount is, you know, left in and they discover, the user discovers afterwards in the survey, you know, that there is that much retained, and it was supposed to have been delivered, so that's a medical event.

But we see this pretty commonly. It's stuck in the vial. It's stuck in the tubing. There was a kink in the tubing.

These types of things are very commonly reported. Various things like that. I can only conjecture, I don't know, but I do hope that the new device that Richard mentioned is indeed an attempt to help with these problems.

MEMBER JADVAR: Thank you.

CHAIRMAN METTER: Thank you, Dr. Ennis and Dr. Jadvar. Any other comments from the subcommittee or questions for Dr. Ennis?

MEMBER OUHIB: This is Zoubir. I have a question and a comment. The question is regarding the time out.

It would be nice to see what exactly was done, or what was not done for some of these medical events. And see if there's a trend somehow in those.

The comment is going back to the infrequent users. And this is sort of like a red flag as we look into expanding some of the procedures to other users.

And we have talked about these in the past. I think that's a, that's sort of something that we really need to keep in mind as, you know, as some of these procedures to be expanded to others.

And then these people will only do one or two every three months, or six months, or perhaps a year and all that. And we can see what the result is as we do such a thing. Thank you.

CHAIRMAN METTER: Thank you, Zoubir. Any other comments? Or questions for Dr. Ennis? Or Dr. Ennis, you have a comment on that?

MEMBER ENNIS: Not only as we know, and as

we've discussed in a sister subcommittee that medical events reporting in general, there are challenges that are not going to be solved any time soon with really getting a full understanding of what happens and other times nothing or not.

So, you know, while it would be great to be able to get more information and drill down, and see whether our recommendations are having an effect, the current way, the system and structure, I think to present that, we'll have to get indirect evidence.

But I do think that Zoubir is implying as well that we, as a group and NRC, need to continue when we go and meet with the various professional societies for example, and we have the opportunity to share this information, we try and drive these things.

CHAIRMAN METTER: Yes, thank you. Do I have any other comments or questions for Dr. Ennis from the subcommittee? How about the committee?

Anybody, any of the NRC staff?

MS. HOWE: Well, this is Dr. Howe. I'd like to make just a quick comment.

Although we put a lot of -- the medical community puts a lot of emphasis on time out, we have had a number of medical events where the time out wasn't effective, because the person that should have

been checking, had something in their mind, and they really didn't look. And they didn't find the error that they had, because they already thought they knew what was going on.

So, it is a good method. But, it doesn't work all the time. Just to add that perspective. Thank you.

CHAIRMAN METTER: Thank you, Dr. Howe. And as we know, that does happen. But, thank you for your comment regarding the time out.

Do I have any other comments from the NRC staff?

(No response.)

CHAIRMAN METTER: Now, Kellee, may I open the line for public comments or questions?

MS. JAMERSON: Norman, this is Kellee.

CHAIRMAN METTER: Yes, Kellee?

MS. JAMERSON: I'll just open the line then. We're ready for the public comments and questions?

CHAIRMAN METTER: Yes.

MS. JAMERSON: Norman or Scott?

CHAIRMAN METTER: I'm sorry, Kellee, what did you say?

MS. JAMERSON: I'm trying to reach the

operator.

CHAIRMAN METTER: Yes.

OPERATOR: We will now begin the question and answer session. If you would like to ask a question, please press star one, unmute your phone, and record your name clearly.

Your name is required to introduce your question. If you need to withdraw your question, press star two.

Again, to ask a question, please press star one. It will take a few moments for the questions to come through, please standby.

CHAIRMAN METTER: Thank you, Norman. Norman, is there anyone on the line in the public that is in line to ask a question?

MS. JAMERSON: There's no comments, Dr. Metter. We can move forward.

CHAIRMAN METTER: Okay. Thank you, Kellee.

OPERATOR: Actually, we did get one question that came through from Tom Conley with the University of Kansas. Go ahead. You may -- your line is now open.

CHAIRMAN METTER: Thank you.

MR. CONLEY: Thank you. This is Tom

Conley. I'm with the University of Kansas Hospital. Not really a question, but a comment.

You were talking about the new SIROS system. We were the second site to receive that. And it is a vast improvement over the old system.

And I do expect to see fewer under-doses and less residual in the tubing. It is a much simpler system.

And I did have a question about it. Since it is a separate system, there's been questions about how the training of physicians to use this new system should go, you know, as far as with the hands on.

Is the -- are the authorized users who are authorized for the, what they're calling the legacy system, are they automatically authorized for this new system?

Or do they have to go through the same level of training that they did for the legacy system? I guess that's my basic question.

CHAIRMAN METTER: Thank you, Mr. Conley. The NRC staff, Lisa, can I -- can you address that?

MS. TAPP: Yes. Dr. Metter, this is Dr. Tapp.

CHAIRMAN METTER: Okay.

MS. TAPP: At this time, we are still

evaluating that specific question.

CHAIRMAN METTER: Okay. Thank you. So when would they -- Dr. Tapp, when do you think that might be available for the users so that they can help to comply with the training and experience?

Would that be an information notice or?

MS. TAPP: Yes. If there's a change, we would have to, which would be requiring more training, we would have to issue either an information notice, or a listserv notice to let members know.

My understanding is that the manufacturer is asking users right now to have additional training, hands on training with that system before they're allowing it to be used.

And I would have to look at the field source and advisory I just received, but I believe that was something that was in place there.

But specifically, do they need all the training that's listed in the licensing guidance? At this point, no, they would not appear to be the case with the current wording in the licensing guidance.

MR. CONLEY: Well, I can tell you that the manufacturer is insisting on training, as far as the hands on training with the device, they are requiring the current authorized users to at least do three in

vitro sessions with this before working with it live.

MS. TAPP: Yes. That's my understanding at this point. But, if they -- the question would be, do they need to do the three inpatient?

At this point, the licensing guidance would not spell out that they would have to do the three patient cases before they would get their final training for the licensing guidance.

MR. CONLEY: Right.

MS. TAPP: Yes.

MR. CONLEY: And actually, at least here, that is what we did. We had -- well, in lieu of the inpatient for the current authorized users, we went with the in vitro, because we really didn't have the system yet. It was training prior to having the system available for patients.

We also do have fellows every year, and what we are doing with them is, we are requiring them to do the full three inpatients for both systems since they will go out of here, and there's no telling which system they're going to end up using.

So, we do the -- we treat them as two separate almost unrelated systems. And train accordingly.

MS. TAPP: That's good to know.

MR. CONLEY: Yes.

CHAIRMAN METTER: Thank you, Mr. Conley for bringing that up. And thank you, Dr. Tapp for your input and for looking at this.

Do I have any other comments or questions from the public?

OPERATOR: No further questions at this time.

CHAIRMAN METTER: Thank you, Norman. Well, it looks like on the agenda we're just about at our break.

So, let us, unless there are other comments before we close for the morning session?

MR. WILLIAMS: Dr. Metter?

CHAIRMAN METTER: Yes?

MR. WILLIAMS: This is Kevin Williams. And I just wanted to say, when you come back from the break, Theresa Clark should be there.

And I'd like to just give her maybe a few minutes just so she could talk to you guys.

CHAIRMAN METTER: Okay.

MR. WILLIAMS: That's when we reconvene.

CHAIRMAN METTER: Okay, Mr. Williams. So, would I just go ahead and let me have you introduce Theresa Clark?

MR. WILLIAMS: Yes.

CHAIRMAN METTER: Okay. Thank -- I will do that. Thank you, for that.

MR. WILLIAMS: Thank you.

CHAIRMAN METTER: No, thank you. So, let's go ahead and convene, and -- recess rather, and reconvene at 11:30, I mean, 12:30.

MS. JAMERSON: Dr. Metter, this is Kellee.

CHAIRMAN METTER: Yes?

MS. JAMERSON: One other thing before we dismiss, is there a motion to accept the subcommittee's report?

CHAIRMAN METTER: Yes, Kellee, thank you for reminding me. Do I have a motion to accept Dr. Ennis' Medical Event subcommittee report?

MEMBER WOLKOV: So moved. This is Harvey Wolkov.

CHAIRMAN METTER: Okay, Dr. Wolkov. Do I have a second?

VICE CHAIR SCHLEIPMAN: Second. This is Dr. Schleipman.

CHAIRMAN METTER: Okay. Thank you for the second. Any discussion?

(No response.)

CHAIRMAN METTER: Okay. All in favor say

aye.

(Chorus of ayes.)

CHAIRMAN METTER: Any abstentions or opposition?

(No response.)

CHAIRMAN METTER: Thank you very much for your vote. And thank you Dr. Ennis for a very nice and informative report.

MR. EINBERG: Yes, and this is Chris Einberg. I would like to also second that. Thank you to Dr. Ennis and the subcommittee for their thorough evaluation and analysis in this area.

And it's greatly appreciated. Thank you.

CHAIRMAN METTER: Thank you, Mr. Einberg. Okay. Any other comments or final words before we close the morning session?

MEMBER OUHIB: Darlene, isn't there on the agenda a non-medical event before the break? Or is the agenda changed?

CHAIRMAN METTER: 11:30 to 12:15 is our break. And we reconvene at 12:15 for the non-medical event.

MEMBER OUHIB: Okay.

CHAIRMAN METTER: Okay. Thank you. All right. So, let's go ahead and recess, and reconvene

at 12:15. Thank you.

(Whereupon, the above-entitled matter went off the record at 11:25 a.m. and resumed at 12:18 p.m.)

OPERATOR: Welcome and thank you for standing by. At this time we will begin our afternoon session.

Again, all participants are in listen only mode during the presentation. When we conduct the question and answer session, please press star and then one to ask a question.

Now, I turn the meeting back over to your host, Darlene Metter. Ma'am, you may begin.

CHAIRMAN METTER: Thank you very much. And welcome back to the afternoon session of the 2020 fall ACMUI meeting.

But before we start, I'd like Mr. Kevin Williams to introduce the new NRC Deputy Director, Ms. Theresa Clark. Mr. Williams?

MR. WILLIAMS: Yes, thank you, Dr. Metter. As I spoke earlier this afternoon, or earlier this morning, I said Mike Layton had retired, and I had the opportunity to take over as the Director.

And along with Theresa Clark who was selected as the Deputy, we're amiss to have an

opportunity to have a couple of words. So, without further ado, I'd like to turn it over to Theresa.

MS. CLARK: Hi. Thanks Kevin. This is Theresa Clark. Hi everyone. I'm sorry that I can't see you in person, but I'm glad to have just a couple of minutes to introduce myself.

My name is Theresa Clark as I already said. I will be coming to join the division from another NMSS division where I've been the deputy director for a few years, and that is the current division of Rulemaking, Environmental, and Financial Support.

So, because I've been part of that division, as well as the prior Division of Rulemaking for a few years, I've had a chance to interact with some of the medical activities that you all touch, like the training and experience issues, and our thoughts on how to address technologies.

And so, I look forward to continuing to work with the committee and with interested members of the public. And I just welcome this experience.

I've had about 16 years of experience at the NRC in a variety of different offices. And I look forward to joining Kevin's team and learning a lot more about what all of you do.

So, thanks.

CHAIRMAN METTER: Thank you very much, Ms. Clark. And we look forward to meeting you in person, hopefully in the near future.

So, to begin our afternoon session, our next presentation is by Mr. Michael Sheetz, our ACMUI member, on non-medical events. And he'll provide some analysis of the 2019 non-medical events reported by medical use facilities and commercial pharmacies.

Mr. Sheets?

MEMBER SHEETZ: Thank you, Dr. Metter. May I have the first slide, please?

So, this presentation will cover the non-medical related events reported by medical licensees for fiscal years '18 and '19. I presented a similar report two years ago for fiscal year '17.

This format for presenting non-medical events was started several years ago by Ralph Lieto, the nuclear medicine physicist on the ACMUI board at the time, and Dr. Donna-Beth Howe, and continued by my predecessor, Dr. Sue Langhorst. I'd like to thank them for setting the stage.

This data comes from the Nuclear Material Events Database or NMED for non-medical events recorded by medical licensees in both NRC and

agreement states.

It does not include the medical events reported under Section 35.45 involving patient exposure errors, Section 35.47 involving unintended exposures to an unborn fetus or nursing infant. Or other events involving patient safety or harm.

What is included are the events reported under various Sections of 10 CFR parts 20, 30, 35, and 49 CFR 171, involving leaking sealed sources, lost or stolen radioactive material, personnel over-exposures, contamination incidents, and transportation incidents involving radioactive material. May I have the next slide, please?

This slide shows the number of non-medical events occurring in the different event categories for fiscal years '18 and '19, ranking them from the most frequent occurring type of event, there were a total of 27 lost, abandoned or stolen sources, 13 leaking sources, eight incidents with the transportation of radioactive material, eight personnel over-exposures, six radioactive contamination incidents, and five equipment malfunctions.

So, on average, there are approximately 30 some non-medical events recorded each year. For comparison, there were approximately 50 medical events

in the medical event category reported each year by medical licensees. May I have the next slide, please?

This chart shows the relative number of non-medical events reported by medical licensees compared to the total number of medical events for all categories.

So, you can see they represent a small portion of approximately 8 percent for combined fiscal years '18 and '19. May I have the next slide, please?

If we look a little closer at the circumstances of the events in the different categories, there are some general recurring themes.

For the sake of everyone's time, I am not going to cover the specific details of each event. I will cover a summary of the events from the most to least frequent in occurrence.

So, for the lost, abandoned, or stolen sources, there were nine involving iodine-125 seeds, approximately 100 to 200 microcuries each, used for radioactive seed localization of non-palpable breast lesions.

Most were lost in the process of removing the seed from the tissue specimen after it had been explanted from the patient, or the seed was left in the specimen and discarded, and one involved a seed

that fell out sometime after being implanted in the patient.

Six events involved the shipment of radioactive material from the manufacturer that were lost by the common carrier, and never received by the licensee. And upon investigation, were never located.

These sources include the Radium-223 source Xofigo dose, Indium-111 octreotide dose to spent moly-tech generators. One spent Iridium-192 HDR source, and ten iodine-125 brachy therapy seeds.

Two events involved iodine-125 or palladium-103 seeds missing following brachy therapy procedures. Three events involved a temporary loss during shipment by common carrier, but then ultimately were recovered or received. These sources include the moly-tech generator, iodine-125 seeds, and Indium-111 dose.

Two events involved mobile abandoned PET containment calibration sources. One from a PET clinic that went bankrupt, and the other from a PET service provider who was not even licensed to hold the sources.

That involved the loss of a 200 microcuries cesium-137 vial source used for calibration for those calibrators, and a mobile

imaging van. One case involved temporary implant using iridium-192 seeds, not iodine-125 seeds as indicated on the slide. That's an error.

The patient removed five strands containing 25 seeds, possibly 19 millicuries. Placed them in the trash. And another four strands containing 20 seeds, approximately 15 millicuries, were flushed down the toilet. The flushed seeds were never recovered.

One event involved the delivery of a Iridium-192 HDR source to the incorrect location at the hospital. It was delivered to the loading dock and not the nuclear medicine department for receipt survey. It was later delivered by the hospital and dock personnel.

And the last event involved the shipment of one vial of lutetium-177, 200 millicuries, but the shipping papers indicated two vials were to be shipped. It was confirmed later that only one vial had been shipped by the supplier. And the next slide, please.

For leaking sealed sources, four involved Iridium-192 HDR sources, found to have removable contamination discovered during source replacement. This activity is most likely due to residual activity

on the service of the source, or the source cable from manufacturing, rather than the source actually leaking activity.

Three events involved cesium-137 dose vial sources found to have removable contamination during their routine six-month leak test. Two events involved iodine-125 seed localization seeds that were cut during removal of seed from the tissue specimen.

Cobalt-57 dose calibrator vial sources found to have removal contamination during the routine six-month leak tests. The strontium-90 intravascular brachytherapy device was found to be leaking by the manufacturer when it was returned by the licensee after the sources had jammed.

A 20 millicurie Cobalt-57 calibration rod source was found to have removable contamination from a leak test performed prior to installation by the service engineer. And a 10 millicurie germanium-68 rod source was broken after being dropped and found to be leaking.

None of these resulted in the spread of significant contaminations. May I have the next slide, please?

For shipments of radioactive material, there were four incidents where the outer surface of

the package containing Technetium-99 radiopharmaceuticals coming from a commercial radiopharmacy had removable contamination above the allowable limits.

In all cases, it was determined that the contamination occurred during packaging at the vendor's facilities. There was no noted contamination of the carriers.

There were two serious vehicle accidents where multiple packages of medical isotopes were thrown from the vehicle. And one driver was seriously injured. In the other case, the driver was actually killed. There was no release of any radioactivity from the packages. And they were all recovered.

There was one event where the carrier reported a damaged package, 200 millicuries of Xenon-133 during transmit. The inner package was found to be intact. And there was no release of radioactivity.

And there was one event where a licensee reported the external radiation level of 200 mR per hour on the surface of a package containing approximately 340 millicuries of Technetium-99m.

A wipe test of the package exterior was performed with negative results. It was discovered that the cover of the lead shield containing the vial

of Tech-99 had separated from the bottom portion of the shielding, resulting in an approximately one centimeter gap of shielding.

It was determined that the radiopharmacist had failed to properly secure the cover for the shielding container. May I have the next slide, please?

For personnel over-exposures, there were three reported over-exposures to personnel from commercial radiopharmaceutical production facilities. Two occurred from the F-18 isotope production. One resulting in a whole-body dose of 50 millisieverts, and one resulting in an extremity dose of 690 millisieverts.

The other event involved an individual working with both moly-tech and germanium/gallium generators, resulting in an extremity dose of 600 millisieverts.

There were two reported over-exposures for nuclear medicine personnel performing clinical procedures. Neither badge readings were believed to represent the actual exposures to the technologist.

It is suspected that the whole-body dose of 130 millisieverts was due to the badge being stored in an area where it was exposed to radiation sources

while not being worn. And the 500 EDE millisieverts expended was suspected to leading to contamination of the ring.

There was an over-exposure to a service engineer from Cyclotron with the PR maintenance activities with an extremity dose of 720 millisieverts.

There was an over-exposure to a researcher using C-11 and F-18 in animal research, with a whole-body dose of 130 millisieverts. It is suspected that some of these doses were due to or attributed to contamination of the whole body badge.

And there was an over-exposure to an interventional radiologist who performed those fluoroscopically guided interventions, NY-90 microsphere cases, resulting in an extremity dose of 530 millisieverts. May I have the next slide, please?

For radioactive contamination, there were two incidents involving contamination of hospital entry areas from patients being admitted who had recently been administered iodine-131 sodium iodide for thyroid cancer therapy but had been released by the licensee. Both events resulted in minor contamination that was contained and ultimately cleaned.

There were two incidents involving contamination of a veterinary clinic, from thyroid treatment of cats with iodine-131 sodium iodide. Actually, this probably should not have been included here, as it doesn't involve human medical use licensees.

There was one case where the patient's shirt was sprayed with approximately 15 millicuries of F-18 FDG during the attempted administration. The patient was reinjected and scanned an hour later, but the images were non-diagnostic from the contamination of a patient.

So, the patient was rescanned an hour later without wearing the contaminated shirt. Skin dose estimates performed by the RSO's indicated approximately two Gray for the patient's skin.

And there was a contamination of a hot lab on a pig and vial containing approximately 270 millicuries of Technetium-99m. It slipped from the technologist's hands, dropped to the floor and broke.

The spill was contained. The tech was decontaminated. And the area was secured to prevent entry to allow for decay of the radioactive contamination. May I have the next slide, please?

For equipment malfunction, there were two

cases reported by the same licensee using a strontium-90 intravascular brachytherapy device where the source train failed to retract from the patient at the end of the treatment time.

One was suspected to leading to incorrect connection to the treatment catheter, and the other due to a kink in the catheter.

There was a case where the HDR source transferred to and was defective and became dislodged from the applicator upon source retraction. The patient treatment had been delivered in accordance with the written directive. The applicator was replaced.

There was a case where the HDR device prematurely terminated the patient treatment, attempts to reinitiate the treatment plan failed. The device was subsequently repaired by the source engineer, and the patient treatment was completed at a later date.

There was an event involving four patients that received higher than normal doses from the breakthrough of strontium-82 from a rubidium-82 generator due to the technologist using Ringer's lactate instead of normal saline to link the generator.

The strontium-82 breakthrough was

calculated to be between two to seven times the allowable limit. May I have the next slide, please?

There are a number of miscellaneous events that get recorded and end then, which do not fit into one of the defined categories. One of these relates to medical licensees with the detection of short-lived medical isotopes at municipal waste landfills or transfer stations.

The radioactivity gets into the waste from the body fluids of patients who have been administered radiopharmaceuticals for diagnostic or therapeutic procedures.

There's no standard reporting requirements for these events. The NRC does not require them to be reported. And so the requirement varies from state to state.

In the past, there has been a relatively large number of events, primarily coming from just a few states. Up until the past couple of years, there have averaged around 100 recorded events annually.

I'm sure many of these events are still occurring across the country. And I totally have gotten feedback from my colleagues that they are occurring across the country.

A response to these events often results

in the waste being held in the garbage truck for a day or two until the radioactivity has decayed away. Or, the contents of the truck are unloaded, and an attempt is made to locate the hot waste bag.

If the bag is located, there may be attempts to identify the originator of the hot waste. Which can then result in a fine or request to rid the waste.

I take the time to point this out, as I feel that these reported events are really only the tip of the iceberg. And that a significant response effort is being undertaken for something that does not present any public safety hazard or risk.

With the increase in use of radiopharmaceutical therapy, I am concerned that this may become an increasing problem with potentially serious impact upon our patients.

Pennsylvania has a model landfill program to address this problem. And that requires all municipal waste to be monitored for radioactive sources.

It allows waste identified too only contain short-lived medical isotopes to be immediately placed in the landfill and buried. This eliminates the response effort for something that does not pose

any risk to the public.

I'm not quite sure on how to address this problem, you know, nationally. So, I would like to make a request or recommendation for the National Materials Program at the NRC and OAS to evaluate this issue.

And hopefully come up with recommendations or guidelines that could be used to educate and advise the state on best practices for processing and disposal of municipal waste identified to contain short-lived medical isotopes. The PA program could be used as a model.

This would be a great benefit for patients who would not need to deal with the threat of fines or penalties from the trash detected to contain small quantities of medical isotopes.

It would also alleviate the need for licensees to instruct their patients to hold their garbage during radiopharmaceutical therapy for several months, which has its own problems. May I have the next slide, please?

So, in conclusion, there's a relatively small number of non-medical events reported by medical licensees. The types of events occurring are not resulting in serious harm to public health and safety.

And while there is a declining number of landfill alarms and response events being reported to NMED, I am concerned that this still presents a problem for patients that warrants investigation.

So, I would like to make a request for recommendation that the National Materials Program evaluate this issue and come up with recommendations or guidelines that could be used to educate and advise the states on best practices for processing and disposal of municipal waste identified to contain short-lived medical isotopes. Thank you.

CHAIRMAN METTER: Thank you, Mr. Sheetz for that very informative summary to the ACMUI and the NRC staff and our licensees.

Do I have any questions from the subcommittee? Or any comments?

(No response.)

CHAIRMAN METTER: Are there any questions from the ACMUI committee itself?

MEMBER OUHIB: Yes, this is Zoubir. Very good presentation. On slide number ten, you had two items that sort of caught my attention.

It said the second and third. Do you know if there was any notices sent out by the manufacturer regarding the, especially the third one, the HDR

device, premature termination of treatment?

Any idea if that was in the report whether the manufacturer sent out a notice to users regarding that?

MEMBER SHEETZ: I do not know if there was a notice from the manufacturer. That was not in the report for that reporting.

MEMBER OUHIB: Okay. Okay.

MR. SHEETZ: And neither for the strontium-90 intravascular brachytherapy device failures. I am not aware of the manufacturer reporting or making any notifications. It's not in the report.

MEMBER OUHIB: Right. Right. I guess the only reason I'm bringing it up is because it's, you know, lessons learned, how can that information be, you know, transmitted to other users so they can avoid having the same situation?

And if there is a need of a service representative to come in and take care of whatever the issue might be, then it would be great.

MEMBER SHEETZ: Well, I guess the -- I'll let the NRC comment. But, just like the medical events that occur and are reported, then these non-medical events, you know, reported by medical

licensees, are also reviewed, you know, by the NRC.

Unless I'm mistaken on that.

CHAIRMAN METTER: Does that help to answer your question, Zoubir?

MEMBER OUHIB: Yeah, yeah. Yeah, that's fine. Thank you though.

CHAIRMAN METTER: Thank you. Mr. Sheetz, I do have a question. I know you mentioned the definition of, you said short lived medical isotopes.

What is our definition of short lived? And then the other question I have is, what do you think the cause of the landfill alarms decrease of the last five years have caused that? It's a significant decrease.

MEMBER SHEETZ: That's a good question. It would be an isotope used for either diagnostic or therapeutic nuclear medicine procedures. Which all would be less than 120-day half-life.

CHAIRMAN METTER: Okay.

MEMBER SHEETZ: And with respect to the decrease in number, you know, starting with fiscal year '16, I'm not sure of that. I'm not sure if they were stop being reported to NMED, because this data is only coming from NMED.

Or if it was actually a decrease in the

number of events occurring, you know, in the agreement states or other states, you know, that would have normally reported that.

MEMBER MARTIN: This is Melissa Martin.

CHAIRMAN METTER: Yes, Melissa?

MEMBER MARTIN: I can tell you, or at least in my experience as an RSO here in southern California. Ours would be a significant decrease in reported events at the landfill sites, because most of our institutions have all spent the money and invested in the portal alarms so that we don't have anything going out of our facilities.

Because it is such an over response required for if you have a Technetium hot diaper that appears at a landfill, it requires such an over response, we invested at the hospitals in enough of the portal alarms so that we don't have hot trash going out.

CHAIRMAN METTER: Thank you.

MEMBER OUHIB: This is Zoubir. I think Melissa makes a very good point. But, you know, if you look at the prostate brachytherapy for instance, there's major, major decrease in that procedure.

And then, you know, there are seeds that will actually accidentally get into the fluid and they

become like in the trash and so on and so forth. And that might, perhaps add to that.

But, because of the major decrease in that procedure, perhaps might have helped also.

CHAIRMAN METTER: Thank you guys. It's just such a striking --

MEMBER OUHIB: Right.

CHAIRMAN METTER: Over the last five years. Yeah.

MEMBER SHEETZ: This is Mike Sheetz again. I think Melissa makes a very good point. In that these events that are being reported could have the origin and the material coming from either the hospital or from a patient's home.

And so, as Melissa said, the -- a lot of the institutions, and my institution included, have radiation monitors that screen all of the red bag and then regular trash. So, we catch this before it would leave our facility.

But, my concern is with the patient. The patient is not going to be able to do that. And I'm concerned with the increase in radiopharmaceutical therapy there are going to be more incidents where the landfill is going to come back to the patient.

And I think the, probably willing to have

to ask the patient to store radioactive waste for several months. And I think the isotope of most concern is iodine-131.

CHAIRMAN METTER: Yes. Well, thank you. Are there any other comments or questions from the ACMUI committee?

Okay. Hearing none, any questions or comments from the NRC staff?

MR. EINBERG: Chris Einberg. I have a question for Zoubir. You mentioned that there's been a major decrease in the prostate brachytherapy procedure.

What do you attribute that decrease to?

MEMBER OUHIB: I'm just going to guess here. Probably people so like apprehensive. Because so many medical events were occurring.

And they just simply did not want to deal with that anymore. There's uncertainty with that procedure per se.

You think you are just absolutely perfect within the gland and all that. And next thing you know, some of the seeds jammed in interior or whatever.

And so really, I think that's probably the major cause. I mean, 2018 I believe or even before,

was not a good year for brachytherapy, period.

There is an interest now to sort of get people trained again. And you know, get onboard and all that. But, I don't see it happening like I thought it might, you know.

Dr. Ennis probably can comment on that one.

MEMBER ENNIS: Well, I mean, it's been a longstanding trend.

MEMBER OUHIB: Yes.

MEMBER ENNIS: And it's hard to answer the question of what the real cause is with any facts. My impression is it's a combination of factors.

One is the medical events definition problem that absolutely had a chilling effect on people. Especially in a therapy that has other alternatives and where while an attractive one, you know, you could easily convince yourself that other alternatives were at least as good, or about as good, or good enough, et cetera.

There's always been competition among the various treatments for prostate cancer. And things tend to go to bed. So, it was a hot one for a while. And now other things have become hot.

That's kind of more of a cultural comment.

But, I think it's true. And you know, I think reimbursement plays a role as well.

The reality is that things are reimbursed better. So, anyone who is choosing to offer this is, you know, willingly giving up on that for greater goals, which is great.

But, as you know, finances have gotten more difficult over the decades, that becomes a little harder to do. So, I think those are the main factors in my perspective.

MEMBER OUHIB: And there's the practical aspect of it, you know. The radiation oncologist is required to go to the OR and all that.

And that's not always easy. You know, while the other procedures like Dr. Ennis was mentioning, you know, IMRT or whatever, you know, it's a lot easier for the radiation oncologist.

MEMBER SHEETZ: Thanks for that excellent insight. And it does show the impacts of our regulations on the practice of medicine.

MEMBER OUHIB: Right.

CHAIRMAN METTER: Thank you. Do I have any other comments or questions from the NRC staff on Mr. Sheetz really excellent presentation?

MR. EINBERG: Chris Einberg again. If

there are no other questions, I wanted to thank Mr. Sheetz, for Dr. Ennis as well for an excellent presentation and for the excellent evaluation and analysis that he performed here. Thank you.

CHAIRMAN METTER: Okay. Norm, is there any comments or questions from the public?

OPERATOR: I do not have any questions in queue. But if they would like to ask a question, they can dial star one and unmute their phone, record their name, and we can prompt them in.

CHAIRMAN METTER: Okay. So, let's just wait a little bit to see if there's anybody that would, from the public that would like to make a comment or a question.

Norman, is there anybody in the queue?

OPERATOR: I have no questions in queue at this time.

CHAIRMAN METTER: Okay. So, if there's no questions from the public or comments, do I have a motion to accept the non-medical events' subcommittee report as presented by Mr. Sheetz?

MS. JAMERSON: Just a minute before you make the motion, I just want to clarify something -- Mr. Sheetz that his recommendation is that the staff and the body make the issue of the detection of short-

lived medical isotopes in municipal waste.

CHAIRMAN METTER: Okay. So, that's included in the motion or --

MS. JAMERSON: Yes. I just wanted to confirm that that was correct. That that's his recommendation for the staff's consideration.

CHAIRMAN METTER: I believe it is. Is that correct, Mr. Sheetz?

MEMBER SHEETZ: Yes. I did make a recommendation that the National Materials Program, or some entity evaluate this issue and come up with some recommendation or guidelines that can be used to educate and advise states on best practices for processing disposal of municipal waste containing short lived medical isotopes.

CHAIRMAN METTER: Okay. So, that will be part of the subcommittee's report and recommendation. So, given that, may I entertain a motion to approve the subcommittee report and recommendation?

MEMBER WOLKOV: So moved. Harvey Wolkov.

CHAIRMAN METTER: Thank you, Mr. Wolkov.

MEMBER MARTIN: I second, Melissa Martin.

CHAIRMAN METTER: Thank you, Melissa. Do I have any further discussion?

MEMBER SHOBER: This is Megan Shober.

There wasn't a subcommittee for this. So there -- was there?

MEMBER SHEETZ: No. There was not. I was going to make that when I specified first.

CHAIRMAN METTER: Oh, I'm sorry.

MEMBER SHEETZ: This is not a subcommittee. This is just a report being presented by an ACMUI member.

CHAIRMAN METTER: Okay. I'm sorry. Thank you, Megan and thank you, Mr. Sheetz for the correction.

So, do I have then -- so any discussion on the non-medical events report?

(No response.)

CHAIRMAN METTER: Okay. All in favor?

(Chorus of ayes.)

CHAIRMAN METTER: Any abstentions or opposition?

MEMBER SHOBER: This is Megan Shober. I'm just not sure what we're -- the motion is for at this point.

CHAIRMAN METTER: The motion is the report that Mr. Sheetz presented on the non-medical events with the recommendation that the staff at NMED evaluate this issue to bring guidelines on the

municipal processing and disposal of radioactive waste.

MEMBER SHOBER: So, it's a recommendation to do -- are you asking to form a subcommittee? Or -- we don't usually just accept his talk.

CHAIRMAN METTER: No.

MEMBER SHOBER: But, what's he asking?

CHAIRMAN METTER: Okay. Mr. Sheetz, do you want to go ahead and re -- clarify this?

MEMBER SHEETZ: Well again, as I stated, I'm not sure of the exact format on how to address this. So, I'm trying to raise this issue to a higher level as opposed to just presenting data and everything goes on as normal.

I am requesting that there be an evaluation of this issue by the Materials Program, or whomever.

Or a notification on this issue being disseminated, again, not sure to whom, in order to bring to light that there is potential problems with how the municipal waste is being screened and handled with respect to the, you know, identification and permanent disposal of the waste that contains short lived medical isotopes.

CHAIRMAN METTER: Megan, I believe that --

MEMBER SHEETZ: That's it, I guess.

CHAIRMAN METTER: I believe --

MEMBER SHEETZ: I'm going to yield to the NRC on how this could go forward at all at this point.

MR. EINBERG: Chris Einberg here. So, what I believe that Mr. Sheetz is recommending is to -- a recommendation to the NRC staff to evaluate short lived medical isotopes and impacts that -- in landfills.

For the National Materials Program and through the NRC to evaluate the impacts of the short lived medical isotopes.

And so, it's the recommendation that we would, again, if accepted, we would take that recommendation and work with our agreement state partners and possibly form a working group to evaluate that aspect.

And that's how I see it eventually playing out. So, the recommendation would be to the NRC staff to do an evaluation.

MEMBER OUHIB: This is Zoubir. And that's assuming there is -- there is not an existing one as we speak. Is that correct? Guidelines for that?

MR. EINBERG: Well, I can't speak to that. There may be. There most likely is. But, we would

have to evaluate the recommendation, you know, do a complete evaluation to see if there's already some guidelines and whether they need to be augmented or not.

CHAIRMAN METTER: Okay. So, what I understand. This is Darlene. That the recommendation is for the NRC staff to evaluate the current issues for short lived radioisotopes in municipal waste. And how the licensee should proceed with handling and disposal of municipal waste in the landfill.

It's just to provide some guidance and see where the current issue -- see what we currently have. And then perhaps modify it for clarity.

Is that correct?

MS. DIMMICK: Hi, Dr. Metter. This is Lisa Dimmick. No, I don't think that quite gets to the -- what Mike was talking about.

And I guess here's why. So, as Melissa Martin said, and this is pretty common, I think, across the country. A lot of medical institutions do have portal alarms installed so that their waste is screened before it leaves to go to the waste disposal site.

So, a lot of the waste that's being triggered at municipal landfills is probably, or it

could be waste coming from patients, from their homes.

And then sometimes there's an effort for the landfills to try to trace where that waste came from. And then hold it or return it, or what have you. And so once patients are released from licensees' control, there is -- it's no longer under the licensee's control, that waste.

So, what I think what Mike is asking for is, for the National Materials Program, because there are differences across the country on how waste alarms and landfills handle this. And the state's different responses to these landfill situations.

So, I think he's asking for there to be maybe an evaluation by the National Materials Program. And either issue, you know, some level of guidance nationally, or some position nationally on how to deal with waste from triggering alarms at the used waste facilities.

Maybe that helps to clarify it a little bit more. So, it's not necessarily waste coming from licensees going to the landfills. That is an older issue that has been addressed quite a while ago with facilities installing portal monitors.

So, I think this is still -- and I think that's in part why there's been some, maybe decreases

perhaps. I don't know. And it's really hard to tell why. It could just be people don't report them so much.

So, I think again, the recommendation is more for the National Materials Program to evaluate it and to see if any -- if the NRC and agreement states collectively have a position, or guidance, or a recommendation for dealing with waste from nuclear medicine patients that might be triggering the municipal alarms.

CHAIRMAN METTER: Well, thank you, Lisa for clarifying.

VICE CHAIR SCHLEIPMAN: Hello, this is Robert Schleipman.

CHAIRMAN METTER: Yes, Robert, Dr. Schleipman?

VICE CHAIR SCHLEIPMAN: So, I believe also Mike, Mr. Sheetz mentioned a best practice. And that perhaps part of that recommendation is to identify best practices, which may include portal monitoring. It may include additional instructions to patients suggested, that sort of thing.

So, and then the slide that we're on, number 11 mentions that there are no standard reporting requirements. So, perhaps that would be

something they would also look at in the recommendation.

CHAIRMAN METTER: Thank you, Dr. Schleipman. Are there any other comments to make on the recommendation? Does that help you, Ms. Shober, Megan? On the recommendation that is being proposed by Mr. Sheetz?

MEMBER SHOBER: This is Megan. Yes, I -- I'm onboard with the -- the motion as a recommendation.

CHAIRMAN METTER: And thank you again for asking the question and for clarification.

Okay. So, I believe I had a fir -- I have a motion and a second. And this was the discussion. Okay.

Any other comments?

MEMBER SHEETZ: This is Mike Sheetz.

CHAIRMAN METTER: Yes, go ahead.

MEMBER SHEETZ: I wanted to thank Ms. Dimmick for her clarifying that. She has it exactly right. And I'm concerned with the way it's coming from patients, you know. From households.

You know, and again, for the -- to look at this and come up with, you know, potential education and best practices. Thank you.

CHAIRMAN METTER: Okay. Thank you. As I hear no other comments, can I go ahead have a -- all in favor of the report as presented and the recommendation, say aye.

(Chorus of ayes.)

CHAIRMAN METTER: Thank you. Any opposition or abstentions?

(No response.)

CHAIRMAN METTER: Thank you. And thank you, Mr. Sheetz for a very thoughtful presentation on non-medical events. And it was a very excellent report again.

Next on the agenda is new drug development and labeling by Mr. Frank Lutterodt from the FDA.

MR. LUTTERODT: Hello everyone. I hope you can hear me.

CHAIRMAN METTER: Yes. We can hear you.

MR. LUTTERODT: Thank you. Good afternoon everyone. My name is Frank Lutterodt and I'm a project manager at the division of imaging and radiation medicine, RDRC.

Today I'm going to talk about a new drug. A new radiopharmaceutical drug development and labeling.

Next slide, please. This is the outline

of my presentation. And I'm going to go over the overview of the drug development process and how we regulate radioactive drugs in basic research, pre-clinical phase, clinical phase and new drug application review and labeling.

Next slide, please. You've probably seen these schematics before. And I wish to point out that this is an oversimplification of the whole process.

But that's, briefly, the drug development process begins with pre-clinical research involving synthesis purification, animal testing. And until the sponsor submits an IND, FDA typically takes 30 days to review an IND. And at the end of the review process a may proceed letter is either issued or ban is placed on pre-clinical safety issues.

Next slide, please. So, I'm going to continue this with talking a little bit about the RDRC program.

The RDRC program began when the FDA published in the federal register classifying all radioactive drugs as either new drugs requiring an investigation, new drug application for investigational use, according to 21 CFR 312 or generally recognized safe and effective when administered and the conditions specified in the RDRC

regulation, 10 CFR 361.

Under the RDRC, the research is considered to be basic science. And it's done for the purpose of advancing scientific knowledge in standard to obtain the basic information regarding the metabolism, human physiology, pathophysiology, and biochemistry.

I also want to point out that FDA's oversight is on the RDRC committee, and that the IRB is the one who has oversight over the clinical studies.

Next slide, please. So, as I said in the beginning, during pre-clinical research there is synthesis and purification. Target affinity, selection, et cetera. And animal testing, PK, proof of concept, toxicity, translation to humans. And throughout all this process, the FDA would normally encourage the sponsors and applicants to meet regularly or to communicate for guidance on the developing product.

And I also want to point out, generally all drugs, biologics, radioactive drugs, go through the similar development process. And the overarching regulation governing drugs also govern biologics too.

And I'm sure you would notice that I keep talking about drugs, drugs, drugs, but all of this

applies to devices.

Next slide, please. During the clinical phase there are several approaches to Phase 1. There is the exploratory IND and then there is the traditional IND.

And basically the INDs are governed by 21 CFR 312. And they are used to established safety, a safety or effectiveness of a drug to support the approval of the new use.

Although all INDs are used to establish safety or effectiveness of the new use of the drug to support approval, the main focus on Phase 1 of the studies is the safety of the drug.

Next slide. So as I mentioned, exploratory IND is basically a clinical trial that is conducted in the early Phase 1. It involves very limited human exposure and has no therapeutic or diagnostic intent.

The main purpose of this approach, normally, is to find a promising drug candidate to enable the sponsor to proceed efficiently with the most promising drugs. So there is not typically the duration of dosing and an exploratory study is expected to be limited to around seven days.

And it's also important to emphasize that

throughout these processes and phases there are many options for continued dialogue with FDA during this process.

Next slide, please. Traditional Phase 1 studies are designed to determine the metabolism and clinical interactions of the drug in humans.

The trial is associated with increasing doses are, if possible, to gain early evidence of effectiveness. And during Phase 1, sufficient information about the drug from clinics and from ecological effects should be obtained to present a design of a well-controlled scientific Phase 2 study.

And typically, it involves a small number of participants. Generally in the range of 20 to 80 subjects.

Next slide, please. During Phase 2 more information is gathered about drug safety and effectiveness in the condition or disease being studied.

And a larger group of subjects or participants are enrolled. And the subjects receiving the drug may be compared with others receiving placebos.

Safety and short-term adverse reactions continue to be evaluated at this stage. And it

usually involves more than several hundred subjects.

Next slide, please. During Phase 3, it's intended to gather additional information about effectiveness and safety that is needed to evaluate overall benefit, risk, relationship of the drug. And to provide an adequate basis for a position and labeling.

Phase 3 usually includes several hundred to several thousand subjects. If safety and efficacy are adequately confirmed during this Phase 3 clinical testing, the studies may end at this point and the NDA new drug application may be submitted to FDA.

Next slide, please. Throughout the phases of development, a sponsor meeting and platform for communication with the agency and for sponsor to give advice, for FDA to give the sponsor advice provided.

And during the review stage, pre-clinical data and data from the clinical trials are reviewed to assist FDA in making the benefit/risk assessment. And the favorable benefit/risk assessment culminates in the review and approval of the drug labeling.

Next slide, please. At this point I would like to get into some terminology about the labeling aspect of this.

And FDA begins reviewing the label, the

teams met and the labeling is revised. And FDA never shares the labeling with the applicant at the time.

And the term, a few things about that. What do you mean by labeling? In general, labeling and label, in general, a label is usually needed on the drug container or package.

And the labeling is written with a written, printed or graphic material accompanying the product. So basically, it's everything else. The labeling has everything else.

Next slide. So the labeling covers the carton and container labels, prescribing information, also known as the package insert, patient labeling.

Typically with patient labeling is medication guide for use of the patient. And then operator guide, in case the drug involve, the use of the drug involves an apparatus or there's an associated apparatus which needs to have a user manual.

The PI, or prescribing information, is written to the prescriber and not the patient. And it should contain a summary of the essential scientific information needed for safe and effective use of the drug and biological product.

The entire drug evolvement process

contributes the data to support the NDA. And the labeling is supported by data in the NDA.

Next slide, please. In 2006 FDA revised the form of the old format of the labeling. And it was known as physician labeling rule, the PLLR format when it was implementing them.

And during that revision, the contents of the PI and the highlights, table of contents and full prescribing information, are revised. And then in 2014 it was further revised to include a pregnant and lactation rule.

The labeling generally must contain the summary of the essential scientific information needed for the safe and effective use of the drug. The labeling must be informative, accurate and neither promotional in terms of false or misleading in any particular way.

In accordance with the regulations, the labeling must be updated when new information becomes available that causes the labeling to become inaccurate, false or misleading.

So all of these revisions are expected to make it easier for the health care practitioner to access, read and use the information in the prescription drug labeling. The revision enhances the

safe and effective use of the prescription drug product and reduces the number of adverse reactions resulting from medication errors as (audio interference) to misunderstood or inaccurately apply the drug information.

So the highlights in the labeling, have a concise summary of important information and a full prescribing information is reorganized according to the clinical relevance.

Next slide, please. So, I had mentioned that in 2014 there was a PLLR. The revision to the Section 8 of the prescribing information.

And the label format was changed to reflect an integrated assessment of known risks relevant to pregnancy, lactation and infertility based on the available information and data.

Next slide, please. Here is a typical table of contents, which mirrors the information organized and the full prescribing information.

You notice that the clinical sections, such as indications, usage and dosage and administration, are ordered first. The chemistry and clinical pharmacology are ordered later in the list.

Next slide, please. So, when FDA approves a product, in addition to the letter of approval there

is an attachment of these package and container labeling. As well as the prescribing information.

And approval of the products does not complete the activity on the drugs. The applicant may file supplements, continue per the safety studies on the IND.

FDA continues manufacturer inspections, active surveillance, and applicant submits periodic safety reports.

So here are a few examples of classes of radiological drugs regulated at CDER. Particularly at the division of imaging and radiation medicine.

We have positron emission tomography generators, scintigraphic agents, magnetic resonance imaging media, ultrasound contrast media, ionic iodinated contrast media, non-ionic iodinated contrast media and non-iodinated contrast media.

And I also need to point out that we also do regulate medical contrast media, radiation medical contrast media products.

In conclusion, the drug discovery and development of new drugs can be long and complicated. From conception to marketing of the drug, FDA encourages the sponsors to meet early in development.

Radiopharmaceutical and PET drugs are

regulated, both under NDA and labeling regulations. Thank you.

CHAIRMAN METTER: Thank you, Mr. Lutterodt, for your presentation and information on the FDA and how they approach these new drugs.

So, do I have any questions from the ACMUI Committee for, on this presentation?

MEMBER OUHIB: This is Zoubir. I'm just curious. You talked about Phase 1, Phase 2 and Phase 3.

By the way, this is an excellent, excellent presentation. I'm just curious about the transition going from Phase 1 to Phase 2, and eventually Phase 2 to Phase 3.

What are the criteria for a product to actually move to the next level?

MR. LUTTERODT: Well, typically Phase 1 studies focus mainly on safety. So, once safety of the drug is established the applicant is free to move on to Phase 2. And normally FDA would encourage a meeting or some kind of communications to discuss the Phase 1 results.

CHAIRMAN METTER: So, this is Darlene Metter. I have a question regarding that transition from Phase 1 to Phase 2.

So does the company that's making the new drug, do they have to then get approval or they just proceed on because Phase 1 has been completed?

MR. LUTTERODT: What typically happens is that the sponsors were the ones that the Phase 1 is completed. Usually there is a meeting.

There is a meeting with FDA. And the Phase 1 results are then discussed. And the sponsor would, at those type of meetings, would indicate their desire to move on to Phase 2 based on the results of Phase 1.

And then during those meetings FDA will provide input on, if there is any service that is needed or not. So typically we do meet with the sponsors before they proceed. Advise them both to do so.

CHAIRMAN METTER: Thank you. Do I have any other questions or comments for Mr. Lutterodt?

MEMBER JADVAR: I have a question. This is Dr. Jadvar.

So, if there is an agent, let's say a radio tracer, I am specifically talking about, let's say Gallium-68 PSMA-11. That is not approved but it has been used globally in numerous publications regarding the safety and efficacy.

Is it possible, and there is no intellectual property ownership by anybody, is it possible to file an IND with FDA for expanded clinical access to agents until there is FDA approved and commercially available, another PSMA based agent?

MR. LUTTERODT: Yes.

MEMBER JADVAR: Okay, good. Thank you.

CHAIRMAN METTER: Thank you for your questions. Any other questions from the Committee?

Okay. Any questions from the NRC Staff? And I'd like to also open up any questions from the public.

THE OPERATOR: And to ask a question, please dial star-1 and then record your name.

CHAIRMAN METTER: Norman, is there anybody in the queue for questions from the public?

THE OPERATOR: We do have a question coming in. One moment while I gather the name.

CHAIRMAN METTER: Thank you.

THE OPERATOR: Our first question comes from Mr. Michael Davis. Sir, your line is now open.

MR. DAVIS: Can you hear me?

CHAIRMAN METTER: Yes, we can hear you.

MR. DAVIS: Yes, I have an old slide that shows the approximate cost of bringing a new drug to

market from discovery through pre-clinical, clinical trials and launched to be $1.7 billion. This was from 2000 to 2002. Do you know of any more recent estimates?

MR. LUTTERODT: I do not know of any recent estimates. I'm sorry.

MR. DAVIS: That's okay. Thank you.

CHAIRMAN METTER: Thank you for that question. Any other questions on the line for the public?

THE OPERATOR: Our next question comes from Mr. John Bullock. Sir, your line is now open.

MR. BULLOCK: Yes, I'd like to ask a question. Is there any FDA approval, do you issue approval letter or anything, when going from Phase 1 to Phase 2 or from Phase 2 to Phase 3?

MR. LUTTERODT: No, there is no FDA approval for transitioning from Phase 1 to Phase 2 or Phase 3. No, there isn't.

MR. BULLOCK: Okay, thank you.

CHAIRMAN METTER: Thank you for that question. Any other questions from the public?

THE OPERATOR: I have no further questions in queue.

CHAIRMAN METTER: Any other questions from

the ACMUI Committee or the NRC Staff?

MEMBER OUHIB: Dr. Metter, I have a question.

CHAIRMAN METTER: Yes.

MEMBER OUHIB: Were there any instances where things went from Phase 1 to Phase 2 and eventually even probably Phase 3, and for some reason something happened and that product has to go back to Phase 1, by any chance, because of some updated data or events that have occurred or reported or whatnot?

MR. LUTTERODT: I recall there was, years ago there was product which an applicant filed a new drug application form. And during the course of the review there were reports in Europe that there was some safety issues with the product.

And in that situation, that product wasn't approved, and FDA encouraged the applicant to come in for a meeting. And the safety issues were looked at very closely for a little bit before the applicant re-filed the NDA.

MEMBER OUHIB: Thank you.

CHAIRMAN METTER: Thank you. Any other final comments? Or questions? Well, thank you very much, Mr. Lutterodt, for that very, very insightful presentation on new drug development and labeling.

So, the final presentation today will be by Dr. Hamby, on dosimetry methodology update for Regulatory Guide 8.39, Phase 2 revision. Dr. Hamby.

MR. HAMBY: Yes, thanks very much. So I'm going to talk about this dosimetry update for Phase 2 of 8.39.

I want to thank ACMUI for letting me talk about this. But I also want to thank the NRC Staff. They've been very responsive and I really appreciate their support in working through this project.

Next slide, please. So what I want to present is the Phase 2 revisions of how we will be suggesting to the NRC, updating dosimetry methods in 8.39.

What we hope to do is provide conservatism. But that we also hope to provide a realistic concern method. Method is going to be based on thresholds, not actually calculating dose per say, but estimating thresholds.

Basic thresholds and also user specific, or patient-specific, thresholds. I think will allow both conservatism but very much, very much realistic methods.

It would be basing estimates on 5 millisievert, 1 millisievert, as the regulation

provides. Also will be looking at breastfeeding infants of the same dose equivalent methods, same limits.

And also something that we can, if you would like, will support emerging technologies. For new methods coming out after the rewrite of the Phase 2, that emerging technologies would fit in very well.

Next, please. So you'll see this graphic a couple of times throughout the talk. Basically, all this is meant to indicate is the two thresholds. The 1 millisievert and 5 millisievert thresholds.

You'll see that the 1 millisievert is related to providing instructions or not, and 5 millisievert threshold is patient release or not.

The area in-between, there are instructions required by the regulation. Instructions for ALARA. Below the 1 millisievert there is no regulatory action required. And then above 5 millisievert there is required to hold patient.

And the way that I will cover this is talking first about basic thresholds and then get into patient-specific thresholds. Where you'll see a lot more specificity.

Next, please. So this is a little bit complicated, agreed. But what I want to do is I want

to focus first on, just straight down the middle.

Display chart, we tried to develop it to help the licensee. I think once you see kind of the, once you look at the flow chart you'll see that it's actually quite simple but it does look a little bit complicated here.

And I'm going to start out by going straight down the middle. And you see basically what this is showing is, threshold comparisons. So A is not the administered activity.

And so we're going to show, basically, do we compare the administered activity to the 5 millisievert, the 1 millisievert thresholds. As long as the patient is not breastfeeding then it makes it a very straightforward process.

As long as the administered activities are less than thresholds or somewhere in between thresholds, then release is appropriate, with appropriate records, of course. So, to begin here I want to go straight down the middle.

Next, please. So this flow chart across the top of the slide basically represents my outline.

I want to talk about dose-rate constants first. And then you'll see that I talk about basic activity thresholds and then specific activity,

patient-specific activity thresholds and breastfeeding. And I'll end with a couple of examples.

So next slide, please. So the first thing we get into is the dose-rate constant. And before I show you that I want to show you essentially the current method.

Dose is essentially calculated this way. I don't mean to talk about the equation so much, but I do want to point out two parameters in the equation.

And that is the gamma exposure constant. The capital Gamma. And the E there is an occupancy factor.

So both of those, the gamma constant is one thing that I will talk about next and what we're planning to do there.

And then the exposure of the occupancy factor, we're going to totally revamp the occupancy factor so that the occupancy factor will be pulled out of this equation, essentially, in our method.

But what this is showing is that, what my intent of showing this is, the gamma constant, if you look at the comment down at the bottom, basically the gamma constant that's in the Reg Guide now, in Rev. 0, Rev. 1, those gamma constants are pulled from many

different sources. And what that means is then there's a potential for the main calculated difference.

And so what we intend to do here is just to standardize that constant. We're going to calculate that constant for error and provide some amount of material around the source, which I'll get into, that provides some level of realism with attenuation. But I want to standardize those. And I'll show you next about the standardization.

Occupancy factors are way too simplistic the way it is. I think there is three or four numbers to choose from. And you want to make that a little bit more real as well.

Next slide, please. So first of all, standardizing the dose-rate constant. We want to provide a consistent method essentially.

And we're going to call this delta PR, and the PR is patient release. Basically to say that this delta is calculated specifically for this reason.

We're going to be calculating point kernels, which is not too different than what's being done now. Except that the point kernel will have an energy threshold specified.

We will be using the nuclear data from

ICRP 107. We'll be considering primary photons, as well as bremsstrahlung, from conversion of say, beta emissions. So, the bremsstrahlung will be built into this as well.

Generally, if you have a fairly strong gamma emitter, the bremsstrahlung contribution is minimal. But you'll see that some of these delta factors are driven by bremsstrahlung. Those nuclides that essentially don't emit primary photons.

We're going to surround, in calculating this point kernel, we're going to go a little bit further to try to provide some more realism here. And we're going to surround the source with two centimeters of tissue.

So about an inch of tissue will allow for attenuation and buildup. We are considering buildup throughout all the calculations.

We allow for attenuation of buildup to say, basically the two centimeters is to say, that's kind of a minimal amount of tissue, at least, that would be covering the source.

And of course, depending on where that source is in the body, the attenuation buildup would be, could be different. It could be more than this. We want to start the process in a way with a minimal,

a nominal amount of tissue to provide some attenuation.

We also want to standardize this calculation of delta for implants. And the implants will be encapsulated, or assumed to be encapsulated, in 50 microns of titanium.

This is primarily for the consideration of bremsstrahlung. The titanium, many of the implants are encapsulated in titanium currently.

Stainless steel is also used. The Z value of atomic number of titanium and stainless are not too far apart. So if we assume 50 microns of titanium, that's going to be very similar of 50 microns of stainless in terms of bremsstrahlung production. Also, generally in terms of attenuation.

But what we're trying to do here is we're sticking to this idea of calculating or starting the whole process with a point kernel, but trying to make sure that we don't, really, the big thing here is to make sure that we don't calculate dose based on very low energy photons.

These photons that would never, never make it out of the body of the patient to expose the bystander. That's photons that never make it out of the body.

But the current method actually would allow for some of this, depending on how the gamma constants is calculated.

Next, please. So this is just to give you, here is a couple of new slides, just to give you kind of an idea of how our calculations currently are comparing to others.

You'll see there is not a lot of difference here. Standardized units of course.

We do have an estimate for ytrrium-90 and lutetium-177. Which are currently not in the, are not in the current Reg Guide. We provided a couple of other references here.

And so you see encapsulation at the bottom. There is a 200 microns of steel estimate and then our 50 microns of titanium, and then none for the others.

And you see all these numbers are very close to, very close to each other.

But what you also see here is that depending on assumptions, these numbers can vary quite a bit. Just looking across in one row, and pick a row, I mean, you'll see that the numbers do vary quite a bit. And so, the standardization of this process.

Next, please. And so now I'm just showing

you this basic activity threshold. And then I'll talk a little bit about basic measurement threshold too. But focusing on activity.

So activity threshold is basically what is the threshold, or what is the activity, administered activity, that will give you the thresholds of 1 millisievert to 5 millisievert.

Next slide, please. So this calculation is done very similar to what's in the current 8.39. This is in Tables 1 and 2.

So I think Table 1 is related to 5 millisievert, Table 2 currently related to 1 millisievert. So we're doing this calculation here not too differently than what is currently available.

Shown in the calculation here, you can use the details I'm hitting, integrated. The details are, is either 5 millisievert or 1 millisievert integrated dose.

And then the only, the other parameters essentially are calculating these point kernels at one meter. And then the other factors are the delta value and then the radiological half-life.

And so I'll just give an example here for Tc-99m. To show that the Q not, which means that, the not is meant to represent the basic threshold. The

most conservative threshold.

So the most conservative threshold here for 5 millisievert integrated dose limited, integrated dose, is 29 gigabecquerels. I'll note that the current Reg Guide says that that number is 28 gigabecquerels. Not a lot of difference at all.

And then the Q not of 1 millisievert is simply going to be factor of five less than that. Because the only thing changing in the equation is the 5 millisievert is changing to 1 millisievert.

So we'll calculate Q not for a number of nuclides. Those nuclides that are currently available in the Reg Guide. And then there is a list of several others, which are either being used or have been noted by the public comment and so forth, but expanding that list.

Next. And then the measurement threshold is just an alternative way, it's currently in the Reg Guide too, but just an alternative way of determining if release or instruction are required. And then I just show, again, the calculation of that threshold.

So you see it for Tc-99m. The M sub 0, M sub 5, is .58 millisievert per hour. Which is very similar to what the current Reg Guide is.

What you notice, maybe, is that the factor

of E, the occupancy factor, is not included in this calculation. The current method of Tables 1 and 2 have this factor of E, occupancy factor, included in the calculations. We've chosen not to do that.

And the reason being is that now Q not and M not are extremely conservative. So this is the most conservative estimate of what the threshold, what could be the administered activity to result in 5, or 1, millisievert.

And if the administered activity is less than these thresholds, than we can be extremely certain that the 5 millisievert, 1 millisievert won't be exceeded. Or if they are, then we know to apply either a hold or we know to apply instruction.

But just very confident in these because they are intended to be very conservative. And then we get into the part about non-conservatism, or trying to reduce conservatism to something more real that will be patient-specific.

Next slide, please. So here's the graphic kind of showing, just in a graphical sense, what happens with these estimates.

So across the top there you see, assume a given nuclide has an instruction threshold, in yellow, at 1.5 gigabecquerels and a release threshold, in red,

of 7.5 gigabecquerels. And then we have an administered activity of 1 gigabecquerels. And then obviously both the one is below both those thresholds and each of the basic thresholds, the very conservative thresholds.

We know then that there is no reason for many regulatory actions being below both thresholds. So a very simple concept, but just graphically to show you how that happens.

Now let's supposed that we increased, for whatever reason, the administered activity must be increased by a factor of ten.

So next slide. If we increase that by a factor of ten, then obviously the 10 gigabecquerels is greater than both thresholds. So we either need to hold that patient, as a licensee, hold that patient until the activity is below 7.5 or we can apply the next level of detail, which is going to be the patient-specific thresholds.

So what we'll do here is we'll take the basic threshold, we will apply specificity to it, in terms of occupancy, in terms of geometry, and also biokinetics, and we will come up with thresholds.

These two, the yellow and the red numbers, we'll come up with modified values for these

thresholds that we'll then instruct the licensee on what to do with the patient that has been administered 10 gigabecquerels, in this case.

So I'll go through that next. Next, please.

All right, so now we're to patient-specific thresholds. These are going to be, these factors are going to develop or implement modifying factors to operate on the basic threshold to develop patient-specific thresholds.

Next. So, essentially what we're going to do now is say, we're going to look at the right side of this, of this flow chart.

And so, essentially we can say, in that first decision box, right down the middle, is A more or less than five, less than the 5 millisievert threshold. And we might answer no here.

And if we answer no, or if we answer no for the next decision box as well, going to this, the large dark blue box there, it says, determine F0 or, F-O, FG and FB. So this is occupancy, geometry and biokinetic factors.

So we're going to determine these factors and then essential reassess where the administered activity sits within our thresholds.

Next, please. So this is what the operation looks like. So Q sub M. So M is going to mean modified.

So the basic threshold of Q not is going to be modified to QM. And it gets modified simply by dividing by FO, FG and FB.

So these factors are all between something greater than zero but equal to or less than one.

If for whatever reason a licensee decided not to consider F sub B, for example, then F sub B remains at a value of 1. If it does, then it's not modifying Q9 obviously.

So, these numbers I have kind of pulled out of the air, that I'm showing here. But I just want to show very quickly how the operation takes place.

So, the idea here is the licensee has looked at the previous graphic, like I showed. Say they're above the thresholds.

So they want to calculate patient-specific occupancy factors, geometry factors, biokinetic factors. And there are the values they come up with. They have to justify those values.

And when the inspector comes in to audit their work, then that's what this justification would

show.

So therefore with a basic threshold of 7.5. The new patient-specific threshold becomes 12. Okay.

And then recalling that our administer activity was ten in this example, then the patient could be released but with instruction. Just as an example in this case. So, the basic threshold simply gets modified by these three factors.

So now what I want to do is I want to talk, a couple of slides each, on each of these factors and show you what our thinking is and how this is going to be proposed.

Next, please. Okay, so I just said this. But you see then, if the factor, the Q sub M of 5 millisievert goes to 12, Q sub M to 1 of 1 millisievert to 2.4.

The ten sits in the middle. Patient can be released, with instruction.

So, occupancy factor. Up in the right corner, just to remind you of the equation that we're looking at here. So we're looking at F sub O.

So the idea is that we would have a fairly comprehensive survey. Or suggest a very comprehensive survey for the licensee.

And I've shown some sample questions here of what might be in that survey. Still developing this.

For example, do you have children, are you breastfeeding, how are you going to return home, so forth. And by taking this survey we will allow the calculation of F not O.

So, one thing I want to say here is that F。 is going to have much more detail to it. Now, recall that if the licensee chooses not to do anything with occupancy, just to say that occupancy is going to be 100 percent of the time, then this value stays at one.

And it's totally the licensee's choice whether they leave it at a value of one or they actually look at the survey, they use the survey to help decide what that occupancy factor should be. And that occupancy factor generally is going to be much less than one.

So the specific conservatisms can be reduced, simply by allowing for this calculation.

Next slide, please. Okay, so look at the left slide of this slide first. So what we're doing here with occupancy factors, we're trying to put a log, the calculational effort up front.

Basically we want to provide a lot of the occupational, or a lot of the calculational rigor. And then try to make it easier for the licensee to apply.

So the idea here is, on the left side we have determined, through the survey, what the patient has taken, we determine that there are potentially two people that could be the maximum bystander.

And the survey indicates that the patient lives alone. And the patient, obviously, therefore doesn't sleep with anybody, won't be around others, can take care of themselves and so forth.

So the two people that could be the highest are the driver, who drives them home. So through a survey we found that they're going to drive home on an eight hour trip. So, there is going to be someone sitting about a meter away for eight hours.

And that's going to be very early after administration, so we want to consider that. When you consider occupancy, we want to consider, does this eight hour trip happen nearly immediately, almost immediately after administration or does it happen three weeks later. And we know that if it happened three weeks later then the impact is going to be much less. So we need to consider, the occupancy, we need

to consider when that occurs. When the occupancy occurs.

And then also the second is, the patient's coworkers. So we've also determined from the survey that the patient is going to go back to work in ten days after administration. And they're going to work half-time.

And also, what we've determined is essentially that two people, that the patient shares an office with someone else. And that person sits about two meters away, for example. So we can consider that.

Sounds like a lot of detail. I think. I hope. Because we're trying to capture that detail to be much more specific. And also, to cut down conservatisms.

Okay, if you look at the right side of the plot, or the right side of the graphic, we have kind of a generic radiopharmaceutical plotted. This is going to be relative external dose rate versus time.

And this is the activity, represents the activity in the patient's body. So this can be completely radiological loss. We can also consider biological loss here or an effective loss.

But at any rate, however we've done this,

we've determined that this is the loss rate, or given rate of the radiopharmaceutical.

So what we want to do, and what the method is going to do here, it's going to take a look at kind of integration. It would be an integration of this activity.

So an integration of dose rate, which would be total dose. Integrate that total dose to a bystander of one meter.

What we're going to do is we'll divide this into thirds. So if you click the button, next. So we're going to divide it into thirds.

The first third is five days. So in the first five days one-third of the total dose is delivered. That basically means total dose to a person standing one meter.

In the next eight days the second third is delivered. And then after 13 days the rest of the dose is delivered.

So the idea here is to determine these five and 13, which is something that would be done ahead of time. We're given pharmaceutical. The licensee can then use this data to determine $F_{\circ}$.

Next slide, please. So if we look at, we'll have a graphic similar to this. Across the top

here we divided that dose into thirds, okay. The dose that is being ultimately delivered by the patient to a bystander. Divided it into thirds, and there is the five days and 13 days.

Now, the first row across there that you see is the driver. If you'll hit the button please?

So the driver is going to exposure by the patient eight hours out of 24. And that eight hours is going to be assumed to occur after administration. Patient has been administered, they get in the car and they drive home.

They see the F_o, occupancy factor, then is calculated as a faction of time, the first day. The one-fifth means there are five days in that first segment. And the one-third is going to be consistent because that means per the dose.

And so what this is showing is, the calculation there shows that the driver is going to receive two percent of the total dose. The total dose potentially emanated by this patient. So we have F_o, .02.

Now if we look at the coworker, we might think to ourselves, the coworker, okay, the coworker is going to be exposed ten days later, half time. And that may or may not be comparable to this.

We want to make sure we capture the maximum bystander. And we also want to make sure that we capture them in a realistic fashion.

So if you'll hit the button. So the coworker is going to be exposed 20 hours out of the week. A total 168 hours in a week. Only exposed while at work. So 20 out of 168, we're working half time remember. Her dose starts in day ten.

And so, the calculation of F_o for them is 20 out of 168. Three eights, so that's three days out of that middle eight days, times a third, and then 20 over 168 times one, one meaning the entire final third is accounted for. And that occupancy factor comes out in .05.

So we've determined that the coworker is going to be the person exposed the most. And we've also determined their occupancy factor, .05 percent.

So, a great deal of realism in terms of what is occupancy factor. We're not just taking a value of one or a value of .25, we're just applying it without a lot of basis.

But we have quite a bit of basis here on how we're applying this factor. The trick for us though is to make this as painless as possible to the licensee.

Now, the licensee is going to have to do this survey and a little bit of work with the survey. But if they want to include the value for occupancy, we're going to try to make that as painless as possible. Do the, mention the calculation.

Next slide. So this just shows you what it might look like for other, considering other potential bystanders. And this would all come from the survey.

Next, please. Geometry factors, just this one slide. Basically, heretofore, geometry has also been point-to-point. And well know that that's not realistic. And so we do want to provide some kind of realism for geometry factor.

You see there is two examples. This is all going to be totally calculational. Total analytical calculation here. But you see, in the first picture, the top picture, we have a point source from the patient irradiating the torso of the bystander at some distance away. This happens to be about the one meter, I think a little bit more than one meter, I think.

So FG, you see in that case is .94. And that .94 compares, it's compared to point-to-point. We considered one point the point. Patient to a point

bystander.

And the picture below shows, okay, now this one has the source distributed throughout the body of the patient. So the entire height of the patient is considered to be uniformly distributed source.

And we're irradiating the bystander, the bystander's entire body. And in that case, the F of G is .79 compared to point-to-point.

So it's all just totally analytical, geometric. But these factors are going to be calculated with distance in mind. You will have a couple of different distances, several different distances.

In fact, what we found, kind of in preliminary calculations, is that once you get beyond two meters, this factor, which is going to be this FG considering distance, once you get beyond about two meters than points work fairly well. Within two meters of each other and this would be, of course, the idea that people are standing a meter apart.

And more importantly that in breastfeeding that the infant is maybe laying on the mother's torso. That those distances are going to be much more important and the FG would be much more important.

Within two meters or so.

Next slide, please. So, final consideration here is F sub B, which is our biokinetic factor essentially. It's a surrogate for the residence time.

And essentially what F sub B is, is a ratio of effective loss to radiological loss. And so you see in the plot on the right side, the radiological loss is in blue. And then if you consider biological loss on top of that you get the plot in orange.

Then what we do is we integrate both and take the ratio. So we see the definition of F sub B is the integral of R(t), which is the retention function, and then divided by, just either minus lambda-T, where lambda is radiological.

And when we do that, what we see is that we can calculate this F sub B as retention function, integration to retention function, times lambda-R. I think you'll see in the next step of slides where the lambda-sub-R comes in. Basically, radiological decay constant.

But F sub B is fairly straightforward. And I'll show you in the next slide how it plays out.

Next. So this is just showing two fairly

simple retention functions. The first one on the left is a single-exponential, the one on the right is a double-exponential. It's two, essentially two compartments. Two loss compartments. And on top of that, it's also radiological loss.

And for the single-exponential retention function you see that F sub B, it just turns out to be a ratio of effective half-life to radiological half-life. And for the case, the double-exponential, it is essentially the same thing but there is two exponential, or two effective half-lives that are weighted. And the weights, F1 and F2 are basically how much is in the, how much is a certain compartment.

So, it turns out to essentially be effective half-life over radiological half-life, so F sub B. But what it does do is it allows the licensee to use a specific retention function, if they have it.

And if they don't, then we will have ways driven in, that are determined, I guess, to determine this retention. Or they can use a simple retention function. As long as the licensee can justify it then the licensee is free to use the retention function that they can basically prove works.

Next slide, please. So what this does here is an example of how F sub B changes. And this

is for iodine-131 and sodium iodide.

And we've had a single-exponential, we have a couple of different functions, retention functions, for hyperthyroidism. And a couple of functions for thyroid cancer.

And what we see is that F sub B can vary quite a bit. An order of magnitude. You see that the value in there is .84 and another value is .084. So nearly an order of magnitude can vary based on the retention function.

We would suggest not tying any one retention function to the Reg Guide, but to allow the, for the licensee to develop their own retention function. As long as they have the data to support it.

Next slide, please. So then the final piece here is breastfeeding activity thresholds and interruption times.

So now we're going to the left side of the flow chart. And you see down the third, we'll start in the middle, go down, the third decision box says, is the patient breastfeeding. And if the answer is yes, then essentially we're going to calculate infant thresholds.

They'll look at our administered activity

and compare it to infant thresholds. And then determine whether or not interruption is necessary.

Next slide, please. So with calculating these thresholds for infant dosimetry, we will still values of, embedded in here, values of F sub G, F sub B and F sub O.

There will be two geometry factors associated with different distances. The two geometry factors basically are a mother's body for radiating the infant versus if activity bio-accumulates in the breast then the breasts would be, maybe a hotter source for the infant. And so that would also be considered F sub G.

Retention functions can be, there is a retention function for the pharmaceutical in this patent, then that can be applied with F sub B. And then also, $F_{\circ}$ is applied in terms of, by showing a 30 minute duration every three hours, what the value would be. That seems to connect a couple of times.

But also if, let's say the mother has been breastfeeding already for a few months and knows what the characteristics are for this infant. How often they feed. They feed 15 minutes every two hours, for example, then they can use that and calculate occupancy factor much more precisely.

For the values of when does first feeding occur and so forth. What's the consumption rate, what's the adsorption rates of activity.

Very likely this F1 value, which is how much is absorbed from the gut of the infant, very likely will remain one. That's a conservatism that's not unreasonable. And then infant dose coefficients taken from various sources calculate internal dose.

So, we'll be calculating external dose from basically two geometries. And then also including internal dosimetry. And in many cases, the internal dosimetry will be the driving force.

Next, please. So this document has already pointed out something here, and I appreciate that comment.

I want to just say, I wanted to show you this slide. Not necessarily to pick on any one number or any one reference, but just to show you that the estimates are varied throughout time, throughout maybe regions of the country. That the estimations are vary.

We don't intent to get into this about specific recommendations guarding cessation, for example. What we would like to do is we would like to show a 5 millisievert and a 1 millisievert threshold

and then allow the licensee to make those decisions about, obviously, if the dose mechanism rate is 5 millisievert, then interruption of cessation must occur. Or there is some waiting period.

But then less than 5 millisievert, greater than 1 or less than 1 millisievert left to allow the licensee to determine where, what interruption times are appropriate. And maybe there are norms with a certain facility, be able to stick with those.

But the intent of the slide is not to say that any one method is, what we would be suggesting. But just to show you that estimates are varied in some cases quite dramatically.

Next slide, please. And then just to wrap-up here, just a couple of examples. In fact, I think I did have two examples.

Next, please. So, the first one is very straightforward. You see the flow chart up in the right corner just showing basically, how does the flow chart.

So here is a 56 year-old-female administered 1.3 gigabecquerels of ytrrium-90. And so the 1.3 compares to the thresholds for ytrrium-90 of 14 gigabecquerels and 68 gigabecquerels.

So we see the number is much less than

thresholds. Much less than the 1 millisievert. And so, based on the regulation, based on 10 CFR 35.75, no regulatory action is necessary.

Now, the facility may, individually, the facility may choose to provide instruction. It's probably not a bad idea to provide instruction and do other things. But as far as the regulation goes, no regulatory action is posed.

Next, please. And so, this one is a little bit more complicated than the previous. So this is iodine-131 administered to a 40 year-old-male 7.4 gigabecquerels. And you see where the 7.4 gigabecquerels sits in terms of the basic thresholds.

Iodine-131, basic thresholds are quite small. So that .062 and .31 gigabecquerels for those thresholds. So we're more than, we're about a factor of 20 higher than the basic thresholds.

So on the surface, this patient cannot be released. But it would behoove the licensee then to go through and calculate patient-specific thresholds, which we'll do in the next slide.

Next. So, I've limited this just for a matter of time, up in the right corner. At the top you'll see the calculation of the modified threshold. Have the .31 and .062 from the previous slide. And

then we've divided by $F_{\circ}$, F0, FG and FB.

And so, in this case, the occupancy factor was determined to be 40 percent, the geometry factor .72 and then the biological, the biokinetic factor of .084. You see in the thresholds come out there for the modified thresholds of 13 and 2.6 gigabecquerels. And the 7.4 sits in between the two, so the patient can be released but with ALARA instructions.

Next, please. And that's it.

CHAIRMAN METTER: Thank you, Dr. Hamby, for your presentation. It's very thorough, and for the update that's being used for Regulatory Guide 8.39, Phase 2 Revision.

Do I have any questions from the ACMUI committee for Dr. Hamby?

MEMBER OUHIB: This is Zoubir. This is a very interesting --

(Audio interference.)

CHAIRMAN METTER: Zoubir, we can't hear you, yeah.

MEMBER OUHIB: Can you hear me now?

CHAIRMAN METTER: Zoubir, can you speak again? We couldn't hear you.

MEMBER OUHIB: Can you hear me now?

CHAIRMAN METTER: Yes, it's better.

MEMBER OUHIB: Okay. I didn't change anything.

This is a very interesting concept. But I do have some concern about the uncertainty when collecting the data. And you will have patients saying, well, I don't know, maybe, I'm not sure, and so on and so forth.

And that could lead to probably some confusion as far as the data collection is concerned. And when things can change, now you could be talking about a factor of two to a factor of five, a factor of ten or not. Any comments on that?

DR. HAMBY: Yes. I guess my thinking is that in that case the onus falls on the licensee, because I think what would have to happen in this case, in this threshold, with this threshold method is there needs to be confidence in the thresholds.

And if there is uncertainty in terms of -- let's say we're thinking only about occupancy. If there's uncertainty about occupancy, then the licensee needs to take that into consideration. And what can the licensee best justify?

I mean, if the patient is saying things like I don't know about that or I can't really answer that question, then that kind of specificity shouldn't

be included. And that would have to fall to the licensee.

MEMBER OUHIB: So there would be like an option, when unsure use the worst scenario.

DR. HAMBY: Sure, yes. And also if very unsure, then don't consider occupancy. And the --

MEMBER OUHIB: Right, right.

DR. HAMBY: -- occupancy factor would just remain as one. Right.

MEMBER OUHIB: Okay. And how was that compared to actual measurements, your methods of evaluating it? Have you run that?

DR. HAMBY: So do you mean like physical measurement with a --

MEMBER OUHIB: Correct, yeah --

DR. HAMBY: -- dose rate --

MEMBER OUHIB: -- with all these assumptions, base activity, you know. What are you off, two percent, five percent, or what?

DR. HAMBY: So, in table 1, so for the, actually for the basic -- this would be table 1 and 2. For the basic thresholds, we have the measurement threshold. And the measurement threshold is going to say if the patient's dose rate is greater than this value on release, then, you know, depending on where

it falls within the thresholds, you either can't release a patient or you need to provide instruction or nothing.

But that measurement threshold is really, the concept there is really no different than what's in the current Reg Guide.

MEMBER OUHIB: Okay. Thank you.

DR. HAMBY: Sure.

CHAIRMAN METTER: Are there any other questions from the committee for Dr. Hamby? Yes --

VICE CHAIR SCHLEIPMAN: Hi, this is Rob Schleipman. Just a comment. First of all, it's great to see SI units (phonetic) presented and not --

(Laughter.)

(Simultaneous speaking.)

VICE CHAIR SCHLEIPMAN: Number two, I think some of the initial distaste of the current Reg Guide were its use of a point source and very limited distance factors. So I think that this is a vast improvement over that.

But it seems like much of this will fall on the licensee as there may be some uncertainty in biokinetic factors and how well they would be able to provide those inputs, particularly with perhaps newer radio tracers.

DR. HAMBY: Yes, that's certainly possible. If it's a new pharmaceutical, emerging pharmaceutical, then it would essentially be up to the facility.

And my thinking is that those facilities that are doing new things, creating these new technologies, would have the resources to study this. And it would seem reasonable that those are the facilities that are actually doing these studies to determine what is the, what are the biokinetics of this new pharmaceutical.

I wouldn't think that, you know, I mean, a large, a very large fraction of the licensees are in facilities that don't do research, that probably don't, very more than likely don't have the resources, wherewithal and so forth, to do the research for biokinetics. And they're probably not the ones that are going to be developing new methods.

So I don't think you get into that problem necessarily where, you know, some facility, some licensee wants to do something new and they don't have the data for it.

And I would, you know, as a private citizen, I would say if you don't have the data for it, then you shouldn't be doing it and to include, you

know, to account for biokinetics in that regard and maybe use a biokinetic factor of one.

CHAIRMAN METTER: Thank you. Any other questions or comments? We are a little past our time. Any --

MEMBER MARTIN: Yes. Sorry. This is Melissa. I just have a couple of questions.

Number one, will the facilities have a choice as to which dosimetry method to use? In other words, can they use the one that is currently in the Reg Guide and continue to use that?

And number two, will you do any set of sort of sample calculations of version 1, version 2? In other words, if you use the updated new method, would you anticipate more patients going home or more patients being required to stay in the hospital? I think that's a big question.

DR. HAMBY: I'll defer to the NRC staff.

MEMBER MARTIN: Well, that's okay. I --

MS. DIMMICK: Hi, it's Lisa Dimmick. So the Reg Guide is an option or one method for a licensee to determine patient release.

MEMBER MARTIN: Right.

MS. DIMMICK: We are still in the early stages of the Phase 2 update, which will be coming to

the ACMUI working group for review and comment.

So, to determine right now what techniques will be provided in the final product and how test practice is addressed going forward, I'm not certain that until we, you know, fully update the document. But there will be time for public comment on it and an opportunity for ACMUI to review it.

But just to note that, again, the Reg Guide isn't, won't be the only way to determine patient release. I mean, it's a tool that will be able to be used. So, I hope that helps.

MEMBER MARTIN: Thank you.

CHAIRMAN METTER: Okay. Thank you. Any last final questions from the committee for the NRC staff?

(Simultaneous speaking.)

MEMBER SHEETZ: I had one question. Thank you for your presentation.

In arriving at an F sub O for occupancy in completing the questionnaire, will the licensee have the latitude to choose what type of F sub O rule D or will in completing the questionnaire it will then produce the new F sub O factor for the licensee? Do you understand what I mean? How much flexibility do we have in completing the questionnaire, and then what

ultimate F sub O can be used? Thank you.

DR. HAMBY: What we hope to do is, like I said, we hope to do a lot of the calculations up front. What we will, what I can envision is we have say an F sub O table with some values that the user could, that the licensee could select with justification, but also have the flexibility, have enough flexibility in the method where the licensee can justify, can back up a calculation that's more specific for an F sub O. And they would be able to use that number.

So, yes, there will be, there would be guidance, kind of a quick way of looking at a chart, for example, and here's guidance on what FO could be or what FO you should use, but also with the flexibility of saying, if you want to put more resources into it and come up with a value that is more realistic for this particular person, then you have that ability.

CHAIRMAN METTER: Thank you. I think there was another question or a comment.

MEMBER OUHIB: Yeah, this is Zoubir. I just have a question, and this is like a -- I'm not sure how to quantify this.

But for the biokinetic factor, looking at

a breastfeeding patient, and I was looking at your number, there's a significant difference. And it almost seems like the authorized user will have to disclose to that patient, you know, what I'm telling you is this is all based on this assumption and this assumption and all that.

And I just don't know how the patient is going to look at that factor and position and say, well, how reliable is this information. And the answer was like, well, it's one way to do it. They can't say this is 100 percent reliable.

And it's a I guess medical practice or whatever. And I'm not really sure if we're crossing the line somewhere.

DR. HAMBY: Well, my immediate feeling there is there's always uncertainty. And I don't think you can ever tell the patient that I know this for sure.

And another thought is there are methods, procedures for determining specific biokinetics for a given patient, you know, given small amount of radioactivity, small amounts of the pharmaceutical up front to determine what is the best administered activity once you start the therapeutic process.

So there will be methods. There will be

ways of determining. And we hope to exploit this. But there will be ways of getting very specific for an individual person. I guess I don't have anything better than that at this stage.

MEMBER OUHIB: Thank you.

CHAIRMAN METTER: Thank you, Dr. Hamby. Any final questions, again, from the committee? Any questions from the NRC staff? And finally, Norman, do you have any public questions?

OPERATOR: I have a couple. And again, to ask a question, please dial star then 1 and record your name. Our first question comes from Mr. Ralph Lieto (phonetic). Sir, your line is now open.

MR. LIETO: Thank you. I have one comment and one question. My comment is I think as this methodology presented by Dr. Hamby, which I find very fascinating, and it seems like he's put a great deal of work into it.

The concern is that the licensees now are all following the current Reg Guide methodology or that in NCRP I think 158. And so all the software, worksheets, spreadsheets, things of that nature are based on that. And to convert to this type of methodology is definitely going to require I think further discussion.

My question is, with your breastfeeding calculations, did it take into account any radionuclide contamination? Specifically, I believe with 123 there has been issues about breast dose for breastfeeding that takes into account radionuclide contamination from I-125.

DR. HAMBY: So that is a, that's an NRC decision I believe. So I'll pass on that question to the NRC. My calculations, our calculations do not.

MR. LIETO: So your calculations are based on essentially the pure radionuclide.

DR. HAMBY: That's correct.

MR. LIETO: Okay. Thank you.

CHAIRMAN METTER: There's another question I believe, Norman, from the public.

OPERATOR: Yeah, our next question comes from Michael Stabin (phonetic). Sir, your line is now open.

DR. STABIN: Excellent analysis and presentation, David. Almost the same question. I was going to note that in the Stabin and Breitz analysis in the year 2000 we recommended cessation for I-123 sodium iodide, and people said, why? And it's the long-lived contaminants in that product. I'm sure the contaminant levels have changed since 2000. But I

would think that all of the pharmaceuticals, that levels of contaminants need to be considered in the calculation. And that may be a challenge, I think.

DR. HAMBY: Yeah. Thanks, Mike.

CHAIRMAN METTER: Thank you for your comment. Are there any other public comments or questions?

OPERATOR: We do have a couple more.

CHAIRMAN METTER: Okay. Thank you.

OPERATOR: The next question or comment comes from Ms. Andrea River (phonetic). Your line is now open.

MS. RIVER: Hi. Regarding breastfeeding specifically, reducing the dose to the infant is very important. And it certainly is a concern of the pregnant person.

The issue is the actual and sometimes lengthy days of suggested cessation are really unrealistic. And I understand that you're putting it in a guidance and not as a synthesis we should know.

But in speaking to the parents, telling them that they need to have a long, drawn out, 21 day or anything at 7 days is unrealistic because the mom may lose the milk, the mom has to buy or rent equipment. She then has to express and pump breast

milk. Then you have questions and huge concerns from families about what do you do with this contaminated breast milk and did I contaminate the pump then if it's rented.

So I just want to let you know after talking to hundreds of women over many years, this is a huge question and concern. They may often go to their physician, and their physician doesn't know. And if the physician is the one having the discussion with the mother, they are going to leave very unsatisfied or dissatisfied.

So I don't know that there's a place in your Reg Guide for this conversation. But those that are counseling the patient need to come up with a, whether a policy of the institution or some other methodology to assuage the feelings of the parents.

And frankly, I never had issues with Dr. Stabin saying cessation after a certain number of days passed, because it was really realistic in terms of ever going back to breastfeeding for the family.

And then the second comment is that your issues that you're bringing up with the radiation exposure for hyperthyroid, hypothyroid, those patients with I-131 versus RAI are longstanding, I'm glad to see that your calculations are beginning to take that

into more account, because issues with some patients, rare, but some patients we've invited them continually back to our medical center for radiation exposure surveys, et cetera, and extensive counseling.

Those are --

DR. HAMBY: Yes, thank you.

CHAIRMAN METTER: Thank you for the comments. The next question from the public, please. And we'll have to wrap up pretty soon.

OPERATOR: Yeah, next is Mr. Jeffrey Siegel. Sir, your line is now open.

DR. SIEGEL: Hello, everybody. Thank you for giving me the opportunity to speak. My comment is I hope all of you realize that this is now 23 years later. This is the fifth reincarnation of this guidance document. So I'd like to congratulate Dr. Hamby, because what he has shown definitively is for 23 years the guidance has been totally wrong.

I have a lot of issues with what he did do. But there's not enough time to go into it. For example, the geometry factor based on line versus point is not any good. The biokinetic factor, okay. Good luck with the occupancy factor. We have 30 publications which obviously have been ignored. This is not time to reinvent the wheel. We know how to

drive it. Thank you very much.

CHAIRMAN METTER: Thank you for your comment. Any other individuals from the public?

OPERATOR: I have no further questions in queue.

CHAIRMAN METTER: Okay. Thank you, Dr. Hamby, for a very interesting discussion on the update of the Regulatory Guide 8.39 and Phase 2 Revision.

DR. HAMBY: Yeah, sure. Thank you.

CHAIRMAN METTER: Thank you. So this looks like the end of our agenda today. And, Kellee, is there anything else we need to do before we close?

MS. JAMERSON: I have nothing further. Chris or Lisa, do you?

MR. EINBERG: Yeah, I have nothing further also. This is Chris.

CHAIRMAN METTER: Okay.

MS. DIMMICK: Hi, this is Lisa Dimmick. I don't have anything else. Thank you.

CHAIRMAN METTER: Okay. Hearing no other additional business, do I have a motion to adjourn for today?

MEMBER WOLKOV: So moved.

CHAIRMAN METTER: And a second, please. And who was that, please, that very nice person?

MEMBER WOLKOV: Harvey Wolkov.

CHAIRMAN METTER: Thank you, Dr. Wolkov. And a second, please.

MEMBER OUHIB: This is Zoubir. I second.

CHAIRMAN METTER: Thank you, Zoubir. And any discussion? Okay. All abstaining or opposing can stay, but other than that, we'll see you tomorrow.

We'll re-adjourn in the morning at 10:00 a.m. for a closed session. And then our open session will begin at 12:15.

Thank you very much, again, for today and for the very interesting discussion and presentations.

(Whereupon, the above-entitled matter went off the record at 2:28 p.m.)