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NUCLEAR REGULATORY COMMISSION

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ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

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PUBLIC MEETING

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THURSDAY,

MARCH 19, 2015

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The meeting was convened in Room T2-B3 of Two White Flint North, 11545 Rockville Pike, Rockville, Maryland, at 8:30 a.m., Bruce R. Thomadsen, Ph.D., ACMUI Chairman, presiding.

MEMBERS PRESENT:

BRUCE R. THOMADSEN, Ph.D., Chairman

PHILIP O. ALDERSON, M.D., Vice Chairman

FRANCIS M. COSTELLO, Agreement State Representative

VASKEN DILSIZIAN, M.D., Nuclear Cardiologist

RONALD D. ENNIS, M.D., Radiation Oncologist

SUSAN M. LANGHORST, Ph.D., Radiation Safety Officer

STEVEN R. MATTMULLER, Nuclear Pharmacist

MICHAEL O'HARA, Ph.D., FDA Representative

CHRISTOPHER J. PALESTRO, M.D., Nuclear Medicine Physician

JOHN J. SUH, M.D., Radiation Oncologist

LAURA M. WEIL, Patients' Rights Advocate

PAT B. ZANZONICO, Ph.D., Nuclear Medicine Physicist

Non-Voting: FRED A. METTLER, JR., M.D.

NRC STAFF PRESENT:

LAURA DUDES, Director, Division of Material Safety, State, Tribal and Rulemaking Programs

DOUGLAS BOLLOCK, Designated Federal Officer

SOPHIE HOLIDAY, Alternate Designated Federal Officer, ACMUI Coordinator

NRC STAFF PRESENT (CONT'D):

MARYANN ABOGUNDE, NMSS/MSTR/MSEB
LUIS BENEVIDES, Ph.D., RES/DSA/RPB
JENNIFER BISHOP, RIII/DNMS/MLB
MARCIA CARPENTIER, OGC/GCHEA/AGCNRP
COLLEEN CASEY, RIII/DNMS/MLB
ASHLEY COCKERHAM, NMSS/MSTR/MSEB
SAID DAIBES, Ph.D., NMSS/MSTR/MSEB
SARA FORSTER, RIII/DNMS/MLB
CASSANDRA FRAZIER, RIII/DNMS/MLB
SANDRA GABRIEL, Ph.D., NMSS/MSTR/MSEB
JOSEPH GIESSNER, RIII/DRP
LATISCHA HANSON, RIV/DNMS/NMSB-A
MICHELLE HAMMOND, RIV/DNMS/NMSB-B
VINCENT HOLAHAN, Ph.D, NMSS/MSTR
DONNA-BETH HOWE, Ph.D., NMSS/MSTR/MSEB
CARDELIA MAUPIN, NMSS/MSTR/RPMB
ANGELA McINTOSH, NMSS/MSTR/MSEB
TONY McMURTRAY, NMSS/MSTR/MSLB
KEVIN NULL, RIII/DNMS/MLB
PATTY PELKE, RIII/DNMS/MLB
LYMARI SEPULVEDA, NMSS/MSTR/MSLB
SAMI SHERBINI, Ph.D., RES/DSA
TOYE SIMMONS, RIII/DNMS/MLB
KATIE TAPP, Ph.D, RES/DSA/RPB

NRC STAFF PRESENT (CONT'D):

FRANK TRAN, RIII/DNMS/MLB

LESTER TRIPP, RI/DNMS/MB

ALSO PRESENT:

BETTE BLANKENSHIP, American Association for Physicists in Medicine

SUE BUNNING, Society of Nuclear Medicine and Molecular Imaging

PETER CRANE, *unaffilitated*

ROBERT DANSEREAU, New York State Department of Health

WILLIAM DAVIDSON, University of Pennsylvania

LYNNE FAIROBENT, American Association for Physicists in Medicine

CAITLIN KUBLER, Society of Nuclear Medicine and Molecular Imaging

JOSH MAILMAN, Society of Nuclear Medicine and Molecular Imaging

RICHARD MARTIN, American Association for Physicists in medicine

MICHAEL PETERS, American College of Radiology

DHEREEN PRASAD, Roswell Park Cancer Center

MICHAEL SHEETZ, University of Pittsburgh

ALSO PRESENT (CONT'D):

CINDY TOMLINSON, American Society for Radiation Oncology

RICHARD WAHL, Mallinckrodt Institute of Radiology

BIN WANG, Walter Reed National Military Medical Center

T-A-B-L-E O-F C-O-N-T-E-N-T-S

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

(8:38 a.m.)

CHAIRMAN THOMADSEN: Thank you one and all for attending.

And I would like to welcome our new member. Dr. Ennis is now official on the Committee. And newly appointed is Dr. Fred Mettler, who'll be taking a position as a diagnostic radiologist.

Welcome. I hope you enjoy your stay with us.

MEMBER METTLER: Thank you.

CHAIRMAN THOMADSEN: And with that, I'll turn it over -- Mr. Bollock, are you the one who is going to be doing the opening?

MR. BOLLOCK: I am.

CHAIRMAN THOMADSEN: Very fine. Please.

MR. BOLLOCK: Thank you. As the Designated Federal Official for this meeting I'm pleased to welcome you to this public meeting of the Advisory Committee on the Medical Uses of Isotopes.

My name is Douglas Bollock. I'm the Branch 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.

Present today as the alternate designated federal officer is Sophie Holiday, our ACMUI coordinator.

This is an announced meeting of the Committee. It is being held in accordance with the rules and regulations of the Federal Advisory Committee Act and Nuclear Regulatory Commission.

This meeting is being transcribed by the NRC and it may also be transcribed or recorded by others. The meeting was announced in the January 27th, 2015 edition of the *Federal Register*, Volume 80, pages 4319 through 4320.

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

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

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

Our Chairman, Dr. Bruce Thomadsen, therapy medical physicist.

CHAIRMAN THOMADSEN: Present.

MR. BOLLOCK: Our Vice Chairman, Dr. Philip Alderson, health care administrator.

VICE CHAIR ALDERSON: Here.

MR. BOLLOCK: Mr. Frank Costello, our Agreement State representative.

MEMBER COSTELLO: Here.

MR. BOLLOCK: Dr. Vasken Dilsizian, our nuclear cardiologist.

MEMBER DILSIZIAN: Present.

MR. BOLLOCK: Dr. Ronald Ennis, radiation oncologist.

MEMBER ENNIS: Here.

MR. BOLLOCK: Dr. Sue Langhorst, radiation safety officer.

MEMBER LANGHORST: Here.

MR. BOLLOCK: Mr. Steve Mattmuller, radiation pharmacist.

MEMBER MATTMULLER: Here.

MR. BOLLOCK: Dr. Michael O'Hara, our FDA representative.

MEMBER O'HARA: Present.

MR. BOLLOCK: Dr. Christopher Palestro, our nuclear medicine physician.

MEMBER PALESTRO: Present.

MR. BOLLOCK: Dr. John Suh, radiation oncologist.

MEMBER SUH: Here.

MR. BOLLOCK: Ms. Laura Weil, our patients' right advocate.

MEMBER WEIL: Here.

MR. BOLLOCK: And Dr. Pat Zanzonico, our nuclear medicine physicist.

MEMBER ZANZONICO: Here.

MR. BOLLOCK: Okay. I've confirmed we have at least six members, and we have a quorum.

At the table we also have Dr. Fred Mettler. Dr. Mettler has been selected as the ACMUI diagnostic radiologist. Dr. Mettler is pending his security clearance, but may participate in the meeting; however, he does not have voting rights at this time.

I'd like to also add that this meeting is being Web cast, and so other individuals may be watching online. We have a bridge line available and the phone number is (888) 864-0940. The passcode to

access the bridge line is 70873#.

Individuals who would like to ask a question or make a comment regarding a specific issue the Committee has discussed should request permission to be recognized by the ACMUI Chairperson, Dr. Bruce Thomadsen. Dr. Thomadsen at his option may entertain comments or questions from members of the public who are participating with us today. Comments and questions are usually addressed by the Committee near the end of the meeting after the Committee has fully discussed the topic. We ask that one person speak at a time as this meeting is also closed-captioned.

I'd also like to add hand-outs and agenda for this meeting are available on the NRC's public Web site.

At this time I'd ask that everyone on the call is not speaking to place their phones on mute. If you do not have the capability to mute your phone, please press star six to utilize the conference line mute and un-mute functions. I would ask everyone to exercise extreme care to ensure that background noise is kept at a minimum as any stray background noise can be very disruptive in a conference call this large.

At this point I'd like to turn the meeting

over to Laura Dudes, Director of the Division of Materials Safety, States, Tribal and Rulemaking Programs for some opening remarks.

MS. DUDES: Good morning.

ALL: Good morning.

MS. DUDES: How's everybody doing? I'm glad I don't have a script.

(Laughter.)

MS. DUDES: And I often forget that this meeting is being webcast, so when I'm sitting here going like this --

(Laughter)

MS. DUDES: So I'm trying to say, okay, make sure you're looking attentive at this. And I'm always attentive to the topics that we have here.

The change of the seating is a little different, but good. At least we still have some balance of where people used to sit.

I want to just confirm, I know the Chair and Doug have welcomed our new members, but also Dr. O'Hara coming in as our FDA representative. I appreciate that. And congratulate Dr. Alderson as our new Vice Chair. So we have had some change since the last meeting.

Doug, although he's been with us since

last February in an acting capacity, I believe, he's now the permanent branch chief for the Medical Safety Branch.

Chris Einberg, who was the former branch chief, has graciously taken over our Agreement State Branch, and so he's part of our team still, but he's doing another function for us now.

Then the other news of change is that this will be my last ACMUI meeting. I have taken a position in Region II in Atlanta. I often tell everyone if you're not aware Sophie has recently relocated to Atlanta, although she still works for us. And I said well, as soon as I found out Sophie was leaving, I had to go to Atlanta as well.

(Laughter.)

MS. DUDES: But really fantastic news about this change is the person coming in to replace me is someone who has done this job for years and years and years in various capacities. It's Josie Piccone. If I'm not sure if you are familiar with her, but she has an extensive background in both medical, health physics, state and tribal programs, rulemaking, and has done -- even though the division has merged and taken on different functions, truthfully Josie has done all of them. And so that

will be a seamless transition. I know she will be very supportive of the Committee and I think you'll enjoy having her. As I sit here and listen to the presentations and I'm fascinated, interested and getting myself educated, she has a very strong background in this area. So it will be very good for the division.

So in opening remarks we've added these open forum parts to the agenda. And this is my last meeting. Unfortunately I won't be able to join you tomorrow. I'm going to get a crown after a root canal, so that's --

(Laughter)

MS. DUDES: But anyways, Pamela Henderson should be here with you tomorrow.

But I feel so lucky to have worked in this division. I told Patty Pelke, who's here from Region III, a few moments ago that I think my life will be so much more linear when I go back to reactors than it has been in the past two years just because any given day, whether it's a brachytherapy treatment or a diagnostic issue or a generator issue that Donna-Beth has taught me all about, patient release, radiography, rulemaking, tribal, your brain shifts gears 10 times a day in this division, and I've truly

enjoyed it.

With respect to this Committee, I would say that I keep encouraging that as much open dialogue, as much direction as you can give the staff, keep it coming and use the open forums. Use your experience. Bring it here and help the staff craft regulations that are supportive of the public health and safety, supportive of the workers, but not intrusive in the practice of medicine. Those are the most difficult issues that we have on any given day is looking at an event that occurred as a result of a treatment that is doing so much good for an individual and balancing how the staff reacts.

And so this is the Committee that can really influence that. Whether it's comments on Part 20 or Part 35 and where we go, how we resolve those things, this is the committee that has the expertise. And the more early discussions we have -- I've always encouraged the staff don't wait and go create something and then say here, Committee, what do you think? Use, within the FACA process, but use, whether it's teleconferences or subcommittees, to get as much early engagement on issues as possible.

So I do want to thank you all very much for helping me understand the line between regulatory

and the practice of medicine and teaching me a little bit. I think I'm smarter now. And I know I will actually be a better patient, hopefully, or a patient advocate having had the opportunity to work with you.

So with that, I will turn it over to the Chair.

CHAIRMAN THOMADSEN: And on behalf of the Committee I can say we've much enjoyed working with you. We've appreciated your openness and your concern. And we will miss you. We wish you well in your new position.

MS. DUDES: Thank you.

CHAIRMAN THOMADSEN: And I'll have to apologize to Dr. O'Hara for not introducing you. You're far enough around the table. It seems like you've been here for a while.

(Laughter.)

CHAIRMAN THOMADSEN: Is this your first -- you were here last meeting.

MEMBER O'HARA: It is the first meeting.

CHAIRMAN THOMADSEN: This is your first meeting. Oh my gosh. Well, welcome definitely to you, too.

MEMBER O'HARA: Thank you.

CHAIRMAN THOMADSEN: And I hope you, like

everybody else, enjoy the work here.

MEMBER O'HARA: I'm sure it will be an experience.

CHAIRMAN THOMADSEN: Yes.

(Laughter.)

CHAIRMAN THOMADSEN: It certainly will be that, yes.

We start out with old business and Ms. Holiday.

MS. HOLIDAY: Good morning, everyone. As I like to say, I know this is your most favorite part of the meeting when we go over our old recommendations and actions.

So to start off, on the screen and in your handouts -- again as Doug said, there are meeting handouts in the back of the room on my left side behind the lady in blue in case you need a handout.

So on the screen we have 2007, and there's nothing different on here than it was in the fall meeting. All these items are included in the current Part 35 rulemaking.

So then we can move on to 2008. And in 2008 the same thing as last September's meeting. All of these are included in the current Part 35 rulemaking with the exception of items 5, 19 and 20.

Those are delayed, meaning they are not included in the current rulemaking.

Then we move on to 2009. Same thing as last meeting. These two items are in the current Part 35 rulemaking.

2010 is not included in this list because we did close all of those items.

For 2011 all of these are included in the Part 35 rulemaking.

And then we move on to 2012. There's only one item and that was to say that ACMUI requested the reporting structure be reviewed on an annual basis. Since this is an ongoing item, that just forever stays open on this list. And we will hear about that from me in this meeting.

So we move on to 2013. 2013, this was when the Committee worked on providing their comments on the current Part 35 rulemaking. So, all of these are included in the Part 35 rulemaking with the exception of items 21 and 25. Twenty-one has to deal with the germanium/gallium-68 generators, which we will hear from Mr. Mattmuller's subcommittee report later on this afternoon. And item 25 was just to reestablish the Rulemaking Subcommittee. As the Committee is aware, when the current Part 35

rulemaking gets ready to go into the draft final stage, that will come back to the Committee for their review. You will also hear more about the rulemaking status from Ms. Neelum Bhalla later on.

So then we move on to 2014. So again for the first item that has to deal with Mr. Mattmuller's subcommittee. Again, we'll hear from them later on today. And for items 10, 11, 12 and 13 this has to deal with the Y-20 Microspheres Medical Event Reporting Criteria Subcommittee report. And staff is currently in the process of reviewing and evaluating those recommendations. As you all are aware, Ms. Cockerham was on rotation during the time, and we have to learn to balance priorities, but we are currently evaluating those recommendations.

You move on to item 17 where Dr. Thomadsen created a task group, if you will, with Mr. Costello and Dr. Langhorst. You will hear from them two presentations after me.

And for item 18 we can close that because we're all here at the spring meeting.

Item 19, Dr. Thomadsen formed the subcommittee to address the AMPR for Part 20. The Committee had a public teleconference on December 10th, 2014 where we received the subcommittee's

report which was endorsed by the full ACMUI. And that report was received in its final form with the minor comments or changes that were suggested during that public teleconference and distributed in January of this year.

Then you move on to item 20. Item 20 had to deal with the time where we had heard about the draft legislation that went to the Appropriations Committee with the Water and Energy Bill. At that time Dr. Thomadsen had asked Dr. Suh and Dr. Welsh, our former ACMUI radiation oncologist, to also work with -- not at that time, but is now our current radiation oncologist, Dr. Ennis, to pair with ASTRO to address providing language to make changes to that bill. That has actually -- let's see, NRC was issued in Section 402 of our appropriations. We were directed to assess our current Part 35.

MS. DUDES: Part 37.

MS. HOLIDAY: Part 37. I'm sorry. Thank you, Laura. So we have been directed to do that assessment. So that I can consider -- item 20 I still would like to keep it open because that means that that bill has not been closed. So it's still out there at this time. Did I say that correctly?

MS. DUDES: Well, I would suggest maybe

that during the meeting if you wanted to reformulate or rethink that action item for a longer-term view -- I think we talked about -- the original draft legislation was challenging and very directive. And now we have a piece of legislation that tells us to see if the source security rule -- do an assessment of it after two years of implementation.

But there may be other issues that the Committee would want to consider around the idea of alternative technologies or source security. And I would leave that up to you. You could close that because the appropriations came and the language was very simple. It just said do a two-year assessment of Part 37. Report back to Congress and then direct the GAO to do an audit with an independent.

So that sort of addresses the immediate issue. But there are broader issues to source security. And I think more for the medical community in terms of the status of alternative technologies, what's viable for various therapies or diagnostics or blood irradiators. So I would suggest you close that item because it was very specific to language if the Committee believes that to be the case, but consider if there's anything else you would like to pursue over this period of time related to source security.

And I guess it's the viability of alternative technologies, but it's also impacts to the medical community if there were to be a different set of security requirements. So I would just leave that back to you.

CHAIRMAN THOMADSEN: And I think that's reasonable to at least talk about. Right now I would entertain a motion to close that item.

MEMBER LANGHORST: So moved.

CHAIRMAN THOMADSEN: We have a motion. Do we have a second?

MEMBER COSTELLO: Second.

CHAIRMAN THOMADSEN: We have a second. Discussion? Yes, Dr. Langhorst?

MEMBER LANGHORST: I think it is a very important topic for this group to take up, and I say that with hesitation because I know who you're going to want to lead that effort.

(Laughter.)

MEMBER LANGHORST: And, yes, I'd be glad to.

(Laughter.)

CHAIRMAN THOMADSEN: Okay. That will come up just a little bit later. Any other discussion? You've already volunteered. Dr.

Langhorst?

MEMBER LANGHORST: I do want to talk about some of the other things, but --

(Simultaneous speaking.)

CHAIRMAN THOMADSEN: We'll come to those, yes. Any other discussion on this motion?

Hearing none, all in favor, say aye?

(Chorus of ayes.)

CHAIRMAN THOMADSEN: Opposed, say no.

(No response)

CHAIRMAN THOMADSEN: Abstentions?

(No response)

CHAIRMAN THOMADSEN: It passes. We'll close that particular item.

MS. HOLIDAY: Excellent. Thank you. Then that brings us to the last item on this chart which is again dealing with the ANPR for Part 20 simply to say that the Full Committee endorsed the subcommittee report.

Are there any comments or questions or concerns with any of these recommendation action charts?

CHAIRMAN THOMADSEN: Dr. Langhorst?

MEMBER LANGHORST: I just wanted to clarify on the 2007-2008 when you say things are part

of the Part 35 rulemaking --

MS. HOLIDAY: Yes.

MEMBER LANGHORST: -- some are not. Like looking at Gamma Knife Perfexion going from 1,000 to 600. So those have been delayed.

MS. HOLIDAY: Yes, items 5, 19 and 22 on the 2008 chart are delayed.

MEMBER LANGHORST: Right. Right. And also that while some of your -- you mentioned that some of our recommendations are part of Part 35, they weren't accepted. For instance, the Committee strongly encouraged that all people with board certifications be approved as authorized individuals whenever their board certification happened. And I don't think that was in the proposed Part 35. And also the fact that the parental administration of betas versus alphas, we suggested that not be separated, but it was in the proposed Part 35. So while they were included, they weren't accepted. So I just want to make those --

MS. HOLIDAY: I'd also like to respond to that and say so when I say they're included in the current Part 35, it's, as you said, not exactly to say that we have accepted them, but as you know, this is still the draft proposed rule. So it's not final

yet. Staff may send it up as certain way and the Commission may come back and say we don't want it like that. But the Rulemaking Group will address all of the recommendations, all of the comments. So there is -- and Neelam will speak to the Committee later on to tell you that the working group is currently addressing all of the comments that we received. As you all know, the comment period ended November 18th of 2014, so that working group is working very vigorously to address all of the comments that were received.

MEMBER LANGHORST: Right. I just wanted to clarify that they were made part of 35, but they weren't all accepted.

MS. HOLIDAY: Absolutely. Absolutely.

Okay. Are there any other comments, questions or concerns regarding these charts?

Doesn't seem to have any. Thank you very much, Ms. Holiday.

MS. HOLIDAY: Great. Thank you.

CHAIRMAN THOMADSEN: And now we have time designated for an open forum where the ACMUI will identify topics of concern that we should think about, maybe include in future meetings. Yes, Dr. Zanzonico?

MEMBER ZANZONICO: Good morning, everyone. I had several issues that came to mind when I saw this agenda topic. The first is the MIRD Committee of the Society of Nuclear Medicine Molecular Imaging. They're going to be publishing a monograph on alpha particle dosimetry. And it's clear from the literature they complied and their review that there's a real future for alpha particle emitters in radionuclide therapy. And it struck me that when the Committee was considering the licensing requirements for radium-223 dichloride.

My recollection was that we, the NRC, stopped short of the licensing requirements across all alpha particle emitters, but rather restricted what was decided specifically to Xofigo. And I think a broader licensing for all alpha emitters consistent with what was decided for Xofigo should be considered, because I think again there will be a real future for alpha particle emitters in nuclide therapy.

CHAIRMAN THOMADSEN: Sophie, can you clarify, was our decision specifically for that particular radiopharmaceutical? I think it was not.

MS. HOLIDAY: If I may direct that --

MEMBER ZANZONICO: I thought there was some discussion to that effect, and correct me if I'm

wrong.

MS. HOLIDAY: If I may direct that to Dr. Howe who's more familiar with radium-223.

CHAIRMAN THOMADSEN: Please.

DR. HOWE: In the Part 35 rulemaking we're addressing alpha emitters used in nuclear medicine in general. When the Xofigo was looked at, it was looked at in particular because it was the only one. And we were looking at its properties and how it could be used. So I do believe the answer is both. We looked at Xofigo and all of the things that we knew about it, and then we're looking at alpha emitters being used primarily for alpha emitters in a more general term for the rulemaking. Does that answer the question?

CHAIRMAN THOMADSEN: Yes, thank you very much, Dr. Howe. And with that it's definitely a topic we should have on the agenda at least to clarify if it's not done. Yes, thank you.

MEMBER ZANZONICO: Understood. So I had several more items.

CHAIRMAN THOMADSEN: Yes?

MEMBER ZANZONICO: One is the propriety and value of dose tracking. In other words, I guess in Europe they characterize it as a smart card where

the cumulative radiation doses received by patients from diagnostic studies is recorded for some purpose. And I think as you are suggesting or -- we should actively engage the staff in timely issues. And I think this is one that if it's not timely yet, will become timely, the issue of whether there's value, propriety, etcetera, etcetera in a dose tracking practice and so forth. It may be a bit broader than usual topics addressed by the NRC, but I think we have an opportunity to make a statement on it and I would encourage the ACMUI to do so.

And perhaps a related issue, there was an editorial several years ago by Hedvig Hricak, who's the chairman of radiology at Memorial, and David Brenner which stopped short of recommending regulatory dose limits for diagnostic imaging procedures. And that might be a companion issue that's worth considering and staking some position on.

And the last item which I'll be speaking about, which is disposition of radioactive cadavers following either brachytherapy or radionuclide therapy. And I was struck as I was researching the topic for my talk about how sparse and, for lack of a better term, ill-defined the regulatory guidance is

on the topic. So I presume, or I hope that my talk today will sort of be the initial effort in formulating, for lack of a better term, more helpful guidelines for disposition of radioactive cadavers. When I originally was looking into it I thought it was simply a non-issue, but there's some technical complexities that warrant further attention. So those would be my suggestions in terms of issues to address in the near future.

CHAIRMAN THOMADSEN: Thank you very much, Dr. Zanzonico.

Do we have other recommendations? Yes, Dr. Mettler.

DR. METTLER: Just on the dose tracking issue, if anybody's starting to look into it, of course the National Academy just had a whole workshop on it and they published a whole document on it recently that included radiology and nuclear medicine and everything else. It's got some issues.

CHAIRMAN THOMADSEN: Yes.

DR. METTLER: The other thing is down the road -- I don't know enough about this, but I've seen research proposals lately about nanotechnologies to go with nuclear medicine therapy. And so people are working on it. And I don't know enough about

nanotechnology to understand exactly what they're doing, but I don't know whether there's any safety issues or regulatory issues that ought to be looked at.

CHAIRMAN THOMADSEN: Very good. I'll put that down definitely. We are working on that at Wisconsin. Yes, good topic.

Any others? Dr. Langhorst?

MEMBER LANGHORST: We will be having a speaker later at this meeting concerning the licensing guidance for Part 35.1000. And that might be something that the Committee would want to take up on some of the older licensing guidance documents to maybe -- if they haven't been brought before us to kind of step through those and see where things stand on those. So that would be my suggestion.

CHAIRMAN THOMADSEN: Very good. Thank you.

VICE CHAIR ALDERSON: Dr. Alderson here. This is a part where I thought maybe Ms. Langhorst was going to explore what she said a few moments ago, but this issue of source security is an area of great interest to me and I support her interest in that. And I think this Committee shouldn't stop discussing it. Even though the Water and Energy Bill has kind

of made it a set-aside momentarily, I think it's a very important issue to discuss going forward.

CHAIRMAN THOMADSEN: Thank you. Any other topics?

(No response.)

CHAIRMAN THOMADSEN: In that case we'll close this part of our discussion, but do keep in mind that these things can come up any time as they rise during the rest of our discussions today.

That brings us to quite a similar topic talking about new discussion and Dr. Langhorst and Mr. Costello will be talking about the potential for additional topical meetings.

MEMBER LANGHORST: Sophie said she would drive my slides, so I appreciate that. And thank you very much.

Next slide. So Dr. Thomadsen asked Mr. Costello and Dr. Davis and I to look at creating a proposal to present to you all this meeting on costs and logistics for additional face-to-face meeting and/or maybe a medical regulatory information conference to present. This has been a challenge. We feel we've had some very valuable discussions on what it would take to develop this, but we maybe have not met your expectation at this meeting.

Next slide. We've discussed who would or should be the target audiences for this meeting between the medical community and regulators. And when I say "medical community," I don't mean to leave out the patient community either. I think they're part of the medical community because they are part of that medical treatment/medical diagnostic discussion.

Perhaps a good place to start is with the organizations associated with the specialty boards that the NRC recognizes and the regulator who are regularly part of the ACMUI.

Next slide, please. And what would be the purpose or objective of such a meeting? We know we want to enhance communications to improve understanding of how the use of radioactive materials and radiation and medicine is different from other uses and how that could or should impact the regulatory controls. Who should decide what would be the specific objective for such a meeting, and would or should each meeting have the same objective?

Next slide, please. In some of my previous talks I've mentioned the NRC's regulatory information conference, otherwise known as the RIC, and last week was the 27th annual meeting of the RIC

that takes place every year here in Washington, D.C. This is NRC's largest annual meeting with about 3,000 participants from more than 30 countries. This meeting began in the late 1980s and only had a few hundred participants at that point in time. It's taken many years and the commitment by the NRC and the participants to build this meeting and develop its importance and its value to the community. The continued commitment is evident by the fact that you can see there are the next three years' meetings dates up on their Web site so people can plan on, yes, this is when this is going to happen each year. And each year it's held I believe at the Marriott, so close to NRC headquarters.

Next slide. The RIC is co-sponsored by the Office of Nuclear Reactor Regulation in the Office of Nuclear Regulatory Research. The meeting's invitation letter states that the program is designed to encourage informal open dialogue about significant NRC ongoing or emerging activities related to the regulation of nuclear power plants and nuclear safety research. Participants have a unique opportunity to interact with their counterparts to gain and share valuable insights and perspectives on safety and security issues facing both the domestic and

international nuclear community.

For this meeting the regulator is the NRC and the regulated community is somewhat focused on reactor licensees and their associated vendors and interests. There may be talks about radioactive material regulations, but they're limited and again with a focus surrounding reactors. A meeting regarding medical use would not seem to mesh well in this meeting because it would be overwhelmed. Okay?

Next slide, please. Another meeting that Mr. Costello and Dr. Daibes and I talked about was the Organization of Agreement States. This meeting is supported by the NRC and already has gathered the regulatory community involved with the medical use of radioactive materials. An additional day might be added to focus on medical us and regulatory control with that group already there.

The meeting is scheduled the same time of the year, August, and moves to different locations. And so you can see a list of where they have been. And this August they'll be in Boston. Thank goodness it wasn't in January.

(Laughter.)

MEMBER LANGHORST: Attendance for this meeting I think is about around 200, but I was not

able to verify that. But I think it's about that order. NRC supports the meeting and travel expenses for one individual from each Agreement State so that all are represented.

Next slide, please. Some other meetings and models that we discussed are listed here that either to model after or to tag onto. So we looked at our own ACMUI meeting, maybe adding a third day to a meeting or having a third separate meeting, but then bringing in the Agreement States. They're not represented here. Excuse me. They're represented but --

(Laughter.)

MEMBER LANGHORST: And the medical community, while there are various groups out there in the audience, it may not be the best way to do that.

NRC conducts rulemaking workshops, but those interactions seem to mostly -- the purpose of those are for information gathering for NRC staff to take back to then make their product. Now there are NRC stakeholder meetings, and that will seem to be focused on one topic like the recent safety culture meetings that happened across the country. And again, NRC kind of takes that back to make their

product. Don't know always how conducive it is for idea exchange. And it's only happening a couple times and then it's done.

Next slide, please. Now, the NRC staff has been doing much in its outreach efforts trying to enhance the communications with medical licensees and regulators, the stakeholder, other regulatory agencies. They're doing this to promote education of themselves on the relevant topics for each of the groups; again an information exchange between licensees and regulators, and trying to encourage the participation of many groups like physicists, RSOs, physicians, scientists, stakeholders and so on. This outreach at professional society meetings and even their participation in providing talks and so on is very important.

This outreach effort is good and should continue, but it leaves it to the NRC staff to interpret the overall medical community's consensus on topics. How should different or competing interests be interpreted? Could a medical regulatory issues meeting provide a forum for these kinds of discussions among the medical community?

I noticed in looking at the RIC, and since putting together our slides I've learned of an example

of an additional meeting that the NRC has developed from the RIC. About 10 years ago the Fuel Cycle Information Exchange meeting started. That's the FCIX. Got to come up with a better acronym than that.

(Laughter.)

MEMBER LANGHORST: And that meets in June each year. It's a smaller group. And that meeting is hosted by the Office of Nuclear Material Safety and Safeguards, Division of Fuel Cycle Safety, Safeguards and Environmental Review. This conference, as it's described on its Web site, provides a forum for NRC staff, industry representatives, licensees, and other stakeholders to discuss regulatory issues of neutral interests related to the nuclear fuel cycle including licensing, certification and inspection of nuclear fuel facilities, for uranium conversion and enrichment, nuclear fuel fabrication and de-conversion of depleted uranium tails.

So because the RIC was too big for that group and they wanted a more manageable group to discuss their issues, could the NMSS consider sponsoring a similar kind of meeting focused on medical use?

Next slide, please. So in discussing the

developments of a medical regulatory information exchange, we kept coming back to baseball. Okay. Maybe that was just me.

(Laughter.)

MEMBER LANGHORST: But if you build it, will they come?

Next slide, please. And would the medical community have a different idea of why we built it? Would licensees be nervous about bringing up challenges for fear of having their inspector show up the next month to inspect on the issue they raised? I believe that's a definition of a chilling effect or turning oneself into cat food.

(Laughter.)

MEMBER LANGHORST: Next slide, please. So if they hope you build it, will they be more willing to participate? We really came to a conclusion that we need to explore the interest in developing and fostering a medical regulatory information exchange that can include our target audience of regulators in the medical community and built it into a meaningful exchange of ideas that can produce medical use regulations that are more in tune and adaptable to supporting patient care.

Next slide, please. As we started we

proposed doing the following: Explore with our regulatory community and our professional organizations their willingness to help develop and participate in a medical regulatory information exchange perhaps added to the annual OAS meeting. OAS, thanks to Mr. Costello and his discussions with them, is willing to explore this idea. But how would such a meeting be sponsored? How should ACMUI be included in the sponsorship of such a meeting?

Next slide, please. Are there issues with other organizations or vendors helping to fund this meeting or should this totally be funded by NRC? How long should it be? Maybe we start with one day tagged onto the OAS meeting. What are the kinds of topics that people want to discuss? How would that program be developed? Could a couple of the professional organizations rotate partnership with the OAS, the NRC, the ACMUI on developing a programming chair? How do we all make it worth participating?

I believe there needs to be a multi-year commitment made to build such a meeting and participation and to develop products from those meetings so that it gives that exchange traction to prove its worth and its value.

Next slide, please. So what does ACMUI think? Would you be willing to discuss these types of questions with your professional organizations and your regulators to explore their interest and gather their ideas?

I've had an opportunity to speak with some folks already. I discussed this topic with the NCRP PAC 4 members; that's the group that is radiation protection and medicine, when they met on Sunday, and they were interested and supportive.

I'm working with the American Association of Physicists in Medicine to discuss this topic at the May CRCPD meeting. That's Council on Radiation Protection Control.

MS. DUDES: Program Directors.

MEMBER LANGHORST: Thank you very much. That's why I always say CRCPD.

I also hope to discuss this topic at the Health Physics Society meeting in July with the medical health physics section.

Would you all be willing to then provide Frank, Said, myself with your feedback from your professional organizations? And we are willing to keep exploring this concept and then report back to you at the fall ACMUI meeting. Thank you very much.

CHAIRMAN THOMADSEN: Thank you, Dr. Langhorst.

Do we have comments from the Committee? Yes, Dr. Ennis?

MEMBER ENNIS: So I think I would support the idea. I think it would be good to try it for a few years and see if it gets some traction, just based on the other examples you gave where they seem to have fulfilled a role for groups that are similar to us, but not ones that we could dovetail with. Certainly I'd be happy to contact ASTRO and find out what their interest would be. I think making it collaborative, as you said, with all the organizations you listed on one of the slides from the design going forward would make it most likely to be successful.

I'm not sure dovetailing with OAS would be as good, because that's one of a dozen stakeholders, so to speak. And maybe something that's more maybe NRC-based or maybe certainly for convenience like the day after an ACMUI meeting or right before might be better. Those are my thoughts.

MEMBER LANGHORST: Thank you very much. I appreciate those. One of the things that the OAS does bring is representation from the Agreement

States that regulate licensees within their State. And they're already there. That's one of the things that was attractive in that way. And while there is something to be said about having a meeting always in the same place where you know you can count on it, the OAS does move around the country, and maybe it needs to be planned out a little farther in advance, but that gives other parts of the medical community around the country opportunity to at least be part of that. So that was one of the reasons -- a couple of the reasons why we felt OAS might be a good at least fit to start with.

CHAIRMAN THOMADSEN: Mr. Costello?

MEMBER COSTELLO: Yes, when you were talking about the RIC a point you made was that the NRC is the sole regulator. Well, that's certainly not true for medical use of radioisotopes. I mean, Agreement States have pushing 90 percent of the licensees in the United States that they regulate. So I think I'm not saying it has to be at the OAS meeting, annual meeting, but involving the OAS I think is an important thing to do because you get the actual regulators there.

Now the NRC has a lead, clearly. NRC develops guidance. NRC develops regulations which

the states piggyback on. But the implementation of that guidance, the implementation of those regulations is also very important. And I think getting feedback from the medical community on how well we're doing in doing that in licensing inspection I think would be useful.

CHAIRMAN THOMADSEN: Thank you. Dr. Alderson?

VICE CHAIR ALDERSON: I'd first of all like to compliment Dr. Langhorst and Mr. Costello on this initiative. I think this is extremely important. During my still relatively short time here, from the very first meeting I was thinking about things like this, and it never quite came into focus. So I strongly support what you're talking about.

I also think we should think a little more broadly because ultimately who is it that determines how medical radiation is used? Well, ultimately it's the doctors who order it. And I think that a very important community is the general physician community, and particularly the people who teach tomorrow's physicians.

So obviously I bring a bias here. I'm a medical school dean. But just next week I'll be going to the Council of Deans meeting, and if we can reach

into that community, if you could convince deans and people who do medical school clerkship development that are medical students around the country need to learn more about radiation and how it's used in medicine and how they as ordering physicians impact that, I think that would be a tremendous plus.

Now they won't come to a one-day meeting. You'll have to go to them, and you may only get an hour. But I think you could make a real impact by getting those sorts of people to think about medical radiation. And then beyond that to even be more aggressive, I'd have to turn to Laura Weil, but ultimately the public. I mean, there's this mysticism that surrounds radiation and its uses in anything, but particularly in medicine because that impacts them. And ultimately if you could eventually develop some sort of approach that could at least help demystify this issue to the public, I think it would also be useful.

CHAIRMAN THOMADSEN: Thank you very much, Philip, for those comments.

Other comments? Dr. Mettler?

DR. METTLER: As a new person I'm a little confused. So how does this fit in with the remit of this Committee?

CHAIRMAN THOMADSEN: With the which?

DR. METTLER: With the remit of this Committee. In other words, it sounds like a really broad thing that is going to cover everything. And this is medical uses of isotopes.

CHAIRMAN THOMADSEN: Correct.

DR. METTLER: And then I heard that it was maybe that the Agreement States could get input about how well they're doing or whatever. So just what I've heard around the table I've got three different things that don't sound the same to me, and I was just wondering. Again, it sounds like a really broad issue that I don't quite -- I wasn't sure about the remit, when I read the remit, how this fits.

CHAIRMAN THOMADSEN: I think that the -- and please correct me, Dr. Langhorst and Mr. Costello -- I think the concept is that this would help provide the NRC with the input and thoughts from the medical community and provide the medical community with the thoughts of the NRC as to what is needed in regulation. Is that correct?

MEMBER LANGHORST: And if you would also include the Agreement States, yes.

CHAIRMAN THOMADSEN: Right. Well, as far as talking about our charge, it would be dealing with

the NRC. And I think that's where this came from, how it fits in with what the job of the ACMUI is.

Mr. Costello?

MEMBER COSTELLO: I think this idea came in large part from Dr. Langhorst's briefing of the Commission last year in which she made the point, a very good point, is that medical is different. The NRC is a very strong technical agency when it comes to nuclear power reactors. In terms of the regulatory agency in that area, it's probably the best in the world, to be honest. However, and our, because I worked for the NRC for many years, our medical background of our staff and the Commission itself is not the same. Not the same. And medical is different because it's such a profound effect on the lives of patients. And correct me if I'm wrong, Sue, but getting more information from the medical community into the NRC, and ultimately all the other regulators, being Agreement States, might mean that we do our job better.

In addition, the medical use of radioisotopes is a rapidly changing field. It's always changed during my career in the business, when we didn't have microspheres and who knows what else? And so I think the ACMUI helps the NRC with that

regard, but if we were to meet -- and however we did it. I'm not sure of the best way to do it. And as Sue mentioned in the beginning we have a lot more questions than answers. If we could go to them and talk to them at ASTRO or other meetings. They could come to us. I'm not sure we've got the answer to that. But I'm trying to explain what the purpose of this is.

DR. METTLER: I guess what I'm hearing now is that the idea originally was to educate the NRC about how things are different. But what I've heard

-- other things are that we have to go out and then educate the rest of the world about other stuff.

MEMBER COSTELLO: I think it's more the other way around. And, Sue, correct me, because you're smarter on this than I am, but I think it's supposed to be a two-way exchange. But the medical community really knows their stuff. And I think the ways that medical is different, if we the regulators; I'm speaking as an Agreement State Representative here, and the NRC can learn how do this very difficult job better -- you know, Laura talked about the fine line between the practice of medicine and regulation. Very difficult. Very difficult thing to understand.

And we often don't get it right. And I think that talking to the people on the other side who provide the medical treatments in a system that I think would help us, the regulators, do our job better.

Did I get close, Sue?

MEMBER LANGHORST: I think you did very well, Frank.

MEMBER COSTELLO: Thank you.

MEMBER LANGHORST: Thank you. The NRC, the Commission has advisory committees on reactor safeguards, but they felt that it was worthwhile to bring together a group of the industry. And like they say on their Web site, the RIC's meeting states that the program is designed to encourage informal, open dialogue about significant NRC ongoing and emerging activities. I think that's the same reason we're looking at what could be gotten from a medical regulatory issue exchange in bringing together more people who are involved, more regulators who are involved and to explore that opportunity of having those dialogues among the regulators and the medical community.

CHAIRMAN THOMADSEN: Dr. Dilsizian?

MEMBER DILSIZIAN: Thank you. Great discussions. I think from the physicians'

perspective there are so many meetings that we attend. It would be very hard I think for most physicians, including medical students and deans, to really have another meeting that they would attend. I really like the idea of the outreach. I think that if the NRC goes to the medical meetings, whether it's radiation oncology, radiology, nuclear medicine, that would be fantastic. And you will also get unique input from those individual societies that may be different. And I think the discussion will be better. So that's just a solution. Probably it will be less expensive and being more directed going to the physicians rather than having them come to a meeting.

CHAIRMAN THOMADSEN: Thank you very much. Dr. Palestro?

MEMBER PALESTRO: That's exactly what I was going to say, that I think that working to improve communication between the medical community and the NRC is an excellent idea. How to implement it can be logistically difficult, but the simplest and maybe the most expedient way of doing it is by having representatives of the NRC attend some of the meetings such as the Society of Nuclear Medicine, maybe ASTRO, RSNA.

The Society of Nuclear Medicine has for

several years run one or two sessions at every meeting with representatives from the FDA and there's been good interchange, and obviously has worked very well. So I think a meeting along those lines, or a session incorporated into these sorts of meetings might be the fastest and maybe even most effective way of improving communication.

CHAIRMAN THOMADSEN: Thank you, Dr. Palestro.

We have a member of the public.

MS. FAIROBENT: Thank you, Dr. Thomadsen. Lynne Fairobent with the American Association of Physicists in Medicine. Just a perspective from someone who has attended 24 of the 27 NRC RICs over the years, and probably as an individual who has brought this topic up in a variety of forums over the years being back in medical over the last 15 years.

The difference in what a RIC does that the normal communication and outreach -- and NRC does send staff and attends many of the professional society meetings and does interact with us on our grounds. What the RIC or a RIC-like meeting would do is allow the individuals in the medical profession who have to interact on the broad licensee community to interact with NRC on a very informal basis to talk

through issues that are pending that is not able to be done in the same manner once a formal rulemaking is in place, or even in a structured rulemaking round table-type discussion. The RIC is very informal.

In many respects tagging it onto the Organization of Agreement States meeting does make a lot of sense. It would be somewhat cost-effective from NRC's perspective because they already pay for one Agreement State regulator to attend that meeting. The other 13 states that are not Agreement States could be reached out to, to also attend. And the reason I'm saying tag it to OAS maybe initially versus the Conference of Radiation Control Program Directors is that although all of the program directors do attend, they're not paid for by NRC. So it's a logistical-type thing.

And, yes, I agree we're not going to get as many physicians perhaps that one might like in doing outreach to a medical professional society, but I do think that you're going to get the medical RSOs there, and they are the bulk of the individuals who on a routine basis have to deal with the licensing actions, the interpretations of the regulation.

And the reason why it's important that the Agreement States are there, and I think the reason

why it's important for ACMUI's presence to be there, is although ACMUI only advises NRC staff, much of what you do does filter back to the Agreement States and into the programs either through their official representative or when they're looking at adoption of compatible regulations. The levels of compatibility are varied through each of the rule. There are not many that are compatibility A or B that are essentially verbatim to NRC. So the States do have a lot of leeway in the use of medical isotopes.

So I do think that until we do one I don't know that we can all say how beneficial it would be. The first couple of RICs were kind of shaky. If you went to the RIC last week or the week before; I forget which week it was, they're blurring, there's a huge difference in the RIC today than the RIC 1 and 2, 26-27 years ago. So I really would like to see an effort. And AAPM is very supportive of involving our membership to this.

As one of the few organizations that attends every Organization of Agreement States meeting, until you're there that meeting is very different. That's the one meeting where there is open discussion in a public forum on issues across the board between NRC as a regulator and their partner

State regulators. And it's a very different discussion than the type of discussion at the Conference of Radiation Control Program Directors.

CHAIRMAN THOMADSEN: Thank you very much, Ms. Fairobent.

I have one question. As you were having your discussions were you able to assess the interest that the NRC has in this type of a program?

MEMBER LANGHORST: I think they're open to listen to what the ACMUI would like to pursue. We did not get into cost because we don't have it very well defined. Maybe I could ask Said to bring in his perspective.

DR. DAIBES: Good morning. We're currently working on the cost-effective plan and see if we can provide more detail to ACMUI. It's somewhat complicated to simply compare the regular RIC to this idea. So that's why we don't have a very detailed cost analysis yet. We're working on it. We wanted to hear your perspective, and based on your perspective then work on that cost-effective plan to provide you details later.

CHAIRMAN THOMADSEN: Okay. Thank you. Dr. Ennis?

MEMBER ENNIS: So, I think we need to

sharpen what our goal is and what our target is, following up with Dr. Mettler. If our target is to really help educate the regulators about the medical perspective and medical knowledge, then we really need to tailor it in a way that is a significant physician component.

If it's about getting all the regulators together and their RSOs together to talk about how things are being implemented and how that is working, that's a different conversation and a different audience. We just need to decide what's necessary or better. Not the same meeting.

CHAIRMAN THOMADSEN: Thank you. Mr. Costello?

MEMBER COSTELLO: Said, thanks for that. I lean toward the former. The Agreement States and RSOs talk to each other a lot. We have a lot of opportunities to interchange, sometimes in a happy way, sometimes less so. But the States talk to each other a lot. And, however, what we don't do is hear from physicians a lot. I don't think I've ever been to a meeting of physicians. I've never been to a meeting of physicians, or I've never been to an ASTRO meeting, or an AAPM meeting. I would think more -- don't you agree with me?

I think I'd like to hear from what the physicians have to say, what the medical physicists have to say, what patient advocates have to say. Agreement States and the NRC and RSOs, we talk a lot. We're somewhat the same group of people. You might meet at HPS meetings. Sometimes we change positions and RSOs become regulators and regulators become RSOs. We have the same educational backgrounds and such. Physicians are a very different group and their concerns are very different, as are medical physicists. And I think we need to hear from them, too.

CHAIRMAN THOMADSEN: Yes, Dr. Alderson?

VICE CHAIR ALDERSON: To follow up on some of my earlier comments, I understand what Dr. Mettler was concerned about and the NRC might be concerned about, and Dr. Thomadsen's issue, are we regulators or educators? Well, I think the NRC is more in the regulations sphere than the education sphere, but I would suggest to you that it's a continuum. Education and regulation are just part of a continuum where the rules are more and more rigid around the people that you're trying to regulate. And so the better informed they are, the more likely you are to have successful regulation.

And I go back again to say somewhere in this; not as the primary focus, but as a spin-off of this effort if you could develop something as simple as a good slide set and give it to people who are going to the Society of Nuclear Medicine or the Council of Deans or other medical meetings and they could talk about the importance of radiation and why it has to be regulated and why people have to know about it, I think you'd make a real contribution.

CHAIRMAN THOMADSEN: Dr. Langhorst?

MEMBER LANGHORST: I would like to emphasize the word that's used for this fuel cycle group, and it's "exchange." So if we were just wanting physicians to train NRC, we'd be asking you to come in and go to some of their training classes to train them. That's not the purpose of this. The purpose is to exchange ideas about how regulations impact medical use. What is the right balance of we'll say NRC- or Agreement State regulatory control versus practice of medicine. And that is always a moving kind of thing.

So I don't think it's just the physicians telling NRC this is what this all means. It's the NRC, it's the Agreement States talking about this is our purpose in regulating. This is our charter. This

is our charge. And we need to work this together to make it a reasonable set of regulations that meet both interests. So I would emphasize the term "exchange."

Now, I think it's also an exchange between the organizations. And, no, I don't see this as being a 3,000-member meeting, because I don't think that would help. But it may be key individuals from these organizations, key physicians who maybe are in the leadership of each organization to help us in this effort of exchange of ideas and that NRC continues with its outreach, too, to be out there to talk to each of the groups. So I'll emphasize the word "exchange."

CHAIRMAN THOMADSEN: Thank you very much. Ms. Dudes?

MS. DUDES: Laura?

MEMBER WEIL: The other Laura.

CHAIRMAN THOMADSEN: One of the Laura's, please.

MEMBER WEIL: Just to play devil's advocate a bit, one could argue that the purpose of this group is to do exactly what you're describing. And I wonder if it might be the most efficient thing for those of us in this group who go to professional

organization meetings to go there, rather than wearing the hat of a member of that professional society, to wear the hat of being a representative of the ACMUI or the NRC and to foster the communication in that context rather than in the context of being the radiation oncologist or an RSO, or whatever, and to bring that information back and to bring information from NRC to the meeting just -- we're already there. And I wonder if that's the first step, to see if we can foster interest in communicating with the NRC that way.

CHAIRMAN THOMADSEN: Thank you. Now the other?

MS. DUDES: Thank you. Well, I think that it's a good dialogue on this subject and I think it's more than I had expected. And I think you asked how the NRC -- what our thoughts on it are. I think the word that you were talking about, "exchange" -- and I was thinking balance and dialogue. And I think Lynne's right; at OAS we have a good dialogue, not only on the issues of the day, but why we're doing something in a certain way. And often the dialogue on ''why'' is the most important exchange of seeking to understand what the regulators' objectives versus the physicians' objectives are.

That being said, our goal is to serve our community and to serve the public in terms of what you think is best in terms of information exchange, education, outreach and transparency. We will try and find a way to do that. That's also in the interest of -- financially responsible. Some of these things are more suited to the nuclear material users than others. Like going to the meetings, I think that's a good idea to get to the physicians.

But maybe it's not a one-size-fits-all. I mean, maybe you have an outreach plan. Maybe that's what comes out of this as you start talking about what types of things can we do for outreach? And it's not having a meeting a year, but it's what's our plan for the year with the ACMUI, with our own staff to get out to the professional meetings? What are our messages for this year? What are the questions? And keep your communication plan as a living document and update it and look for different ways. Because I mean, budgets are shrinking all around us now, so the fact that we use multiple avenues to achieve a set of agreed upon objectives, I think that's where this conversation is sort of leading us.

CHAIRMAN THOMADSEN: Dr. Mettler?

DR. METTLER: You know most physicians

are just buried in clinical work from morning until night, and they're not going to -- if they go to a big meeting, they're not going to go to something, sorry, that an NRC person shows up and says I'm here to communicate. I mean, they might go if they know the NRC's about to like do something horrible that's going to shut down their practice.

(Laughter.)

DR. METTLER: But I mean, they're just typically going to go to some other part of the meeting.

But if you're really thinking about doing something and you want input back, and you want to do it cheaply, I mean one way is to just put an article in the *Journal of Nuclear Medicine* or an editorial or something that says this is what the NRC is fiddling with and does anybody have any comments? I mean, everybody's going to read the *Journal of Nuclear Medicine* who's in nuclear medicine and they'll say, a-ha, I read that and here's the six things they're up to and, boom, yes, I'll write them an email. So that doesn't cost any money and you'll get to a lot of people. So, I don't know.

MS. DUDES: That's good. Thank you.

CHAIRMAN THOMADSEN: Thank you very much.

We have another member of the public.

MR. PETERS: Yes, Mike Peters, American College of Radiology. I just want to point out, go on record in saying that NRC is certainly one of the best in the Federal Government at stakeholder outreach, and they do a lot of the things already that you guys are talking about here, so it might be worthwhile to explore what they already do within their existing outreach activities.

But the other thing that I wanted to point out is the example of another agency called the Office of National Coordinator for HIT in HHS. And what they do is they have an online forum where they do informal requests for comment when a pressing issue comes up. And the casual nature of it allows them to not have to notice in the *Federal Register* or do something more formal, but it allows them to reach out to various communities.

One other option might be a Webinar series that you can do jointly with the societies. And that way you could reach all the different audiences that you're talking about here and not have to deal with time constraints of physicians and others. And if you attach CME to some of those activities, then that's obviously a good incentive to

participate.

CHAIRMAN THOMADSEN: Thank you. Dr. Suh?

MEMBER SUH: So first I want to thank Sue and Frank for putting this together. I think it's a very timely topic.

Just to kind of emphasize what Laura mentioned, I think one of the things I'm hearing, just because there's a lot of differing opinions of what this should look like, is what is the 'why' behind doing this? It's still not clear to me. Is it an exchange of ideas with the physicians, the public, other stakeholders, the societies, or is it more general dialogue or exchange, as Sue put it, among the various programs, is it to educate? I think one of the things that I think is going to be very important to put some teeth behind this ''what'' is the clear objective of what we're trying to accomplish here? I think this is a good starting point. There's a lot of good discussion, but right now it's a little nebulous to me in terms of what is the clear direction we want to take this.

Because it's very, very large and the question is do we start small and go to societies and have -- just take radiation oncologists, for instance, a presentation by ASTRO, say we'd like to

have a little special forum for those interested in learning more about the NRC and what it involves, what it entails and what it can perhaps provide for you. Try that forum to see what type of interest we get. And if we can put that out there and we have exactly -- if Ron's the only other person who shows up, then --

(Laughter)

MEMBER SUH: On the other hand, if there's a lot of people who show up because there's various topics that are of concern to them, then I think you have a more -- actually, I think the 'why' question I think is very important right now. I think it's a good starting point, but I'm hearing a lot of different things right now.

CHAIRMAN THOMADSEN: Thank you, Dr. Suh. Further comments? Yes, Dr. Langhorst?

MEMBER LANGHORST: That was why it was difficult to come back with something with cost associated with it, because it is potentially very big, but how do you get that dialogue going?

So I really appreciate all the great ideas. And I think I'm showing my age, that I never even thought about Webinar kind of things. So I thought that was a very interesting idea to be

thinking about, too. I like the ideas of perhaps expanding the outreach with various professional societies like maybe a forum. So I really appreciate all your brain power that you've lent to this.

CHAIRMAN THOMADSEN: Thank you very much. And thank both of you for the work you've put into this. I think I would ask you not to step down yet, but to take some of the suggestions that have come out of this discussion and come back to this group with a more refined and complete recommendation of where you think we should go considering all the possibilities of a one-day meeting in conjunction with some other meeting or going in a more limited way to some of the various meetings that will be out there to have a less formal exchange of ideas.

MEMBER LANGHORST: I will commit us to putting together a list of questions for you all to maybe consider. You may not use all of them, but I will start with our small group to develop those and then send them out to the whole group and get your feedback on whether they meet your needs in discussing with your various groups, and would appreciate feedback on that as we prepare for our fall meeting.

DR. METTLER: But you'll articulate exactly what the problem is that you're fixing?

CHAIRMAN THOMADSEN: I think that's the first order of business, yes.

DR. METTLER: Well, thank you very much.

MEMBER LANGHORST: Thank you.

CHAIRMAN THOMADSEN: At this time we are scheduled for a break. We will be back here at 10:15.

(Whereupon, the above-entitled matter went off the record at 10:00 a.m. and resumed at 10:15 a.m.)

CHAIR THOMADSEN: Now I think we have an update from a potential research project that the NRC has been discussing with us on patient release. And Ms. Cockerham and Dr. Howe will be presenting.

MS. COCKERHAM: Good morning.

Quick point of clarification, there is a research project going on with patient release, but that is over in Research; this isn't it. I want to talk to you about something a little bit different.

So, that's going on with Research and, yes, that's on its own path. So, if you want to go to the first slide.

So, what I'm going to talk about is Commission direction that we got in 2014 which the research stuff, I believe, we got in 2012, '11, yes,

further back.

So, this is the most recent Commission direction which they basically added on. So, in addition to what you're doing in research space, please look at these things as well.

So, I'm going to go over the current status, sort of what we're looking at this year and then where we're going on a path forward.

Next slide? Thank you.

So, the tasks that we have now are to -- so this is April 2014, the Commission gave staff direction to verify assumptions made concerning the patient release guidance. And one thing they wanted us to look at is, could we have a brochure?

And is this an NRC brochure? Is this something that a professional society or organization has already created that we endorse? You know, let's look into could we have a small pamphlet that has information on patient release.

They gave us direction to develop a website and they wanted it to provide information to relevant medical organizations, patient advocacy groups. And this would enable patients to access clear and consistent information regarding, you know,

what the radioactive iodine is, how it's used in treatment, how to prepare, what to expect, side effects, some basic radiation safety and precautions to take after receiving the treatment and the risk to others.

They also wanted us to look at guidelines and to develop a standard set of guidelines that licensees can use to provide instructions to patients. And they said that this could be done in conjunction with updates to our guidance and the main two guidance documents we have are Regulatory Guide 8.39 and NUREG-1556, Volume 9.

Then they also wanted us to look at the potential for rulemaking and, like I mentioned, the guidance, we would update that.

Next slide, please?

So, I'm going to turn it over to Donna-Beth. Right now, I'm the Project Manager for this, so I'm looking at the big picture, where we are on a multi-year time line and Donna-Beth is doing the technical lead pieces and worked specifically most recently on the OMB clearance that we need in order to get this information to do the project.

So, I'm going to turn it over to Dr. Howe.

DR. HOWE: So, the Commission asked us to a lot of things. And when they asked to do it, they asked us to go out and get as much information from as broad a stakeholder representation as we could, which would be patients, patient advocacy group, physicians, Agreement States, NRC licensees, professional societies and all people that would be interested in the administration of I-131.

Well, you can't just out and ask people for information. If you're part of the Federal Government, you have to ask permission from the Office of Management and Budget (OMB). So, we needed to get an OMB clearance.

The other thing we did is we split the project into two parts. We looked at the guidance part and we looked at the rulemaking part and we split it so that the first part we're going to tackle is going to be the guidance part; and later, we're going to be tackling the rulemaking.

We felt if we put both of them together, everyone has interest in rulemaking and gets very excited about where we might go in rulemaking. So, we felt the guidance would probably not get as much attention and we wouldn't get as much good information

on that side.

So, I drafted a straw Federal Register notice for the questions that we want to go out and ask because when you're doing OMB guidance, you don't really start at the beginning, you start at the end. And once you start at the end, you know what kind of questions you're going to ask, then you know what you have to go out with and you back it up to where you're asking OMB for permission.

So, for the straw Federal Register notice, I went to Ms. Weil and I went to Dr. Palestro because they are nuclear medicine physicians and are patient advocates to see where I could improve on the straw-man and I got very good input from both of them.

So, then I drafted up the Federal Register notice and the Federal Register notice was published March 3rd. The public has 60 days to respond. This Federal Register notice is not the questions, it is just has NRC -- is NRC looking for the right information? Are we going about it in the right manner? Are we doing it in an efficient manner? And have we estimated the burden on the public to respond to the future Federal Register notice?

So, right now, we're in the 60 day comment

period for that.

OMB has started a new process and that is that while we're in the 60 day comment period, NRC has to go out to nine individuals, and in this case an individual can be a person, it can be a licensee, it can be a professional group, it can be any entity, and ask them the same four questions that we're asking in the Federal Register notice that we just published in March.

And that is, is NRC collecting information? Do they need the information? Is there a better way of collecting it? Have they estimated the burden correctly?

And so, I'm in the process of going out to nine individuals. I've got an individual that represents patients. I've got a patient advocacy group. I've got small clinical facilities around the country, both in Agreement States and NRC States that I'm going to be going to. And I've got one private practice physician in the middle of the country that I'm going to be going to and asking them to evaluate.

The Federal Register notice is really two documents. One is the Federal Register notice which is not very informative. The second is a supplemental

statement. And the supplemental statement is an extraction from the future Federal Register notice that I'm going to be putting out. And it essentially states why we need the information in general terms what we're going to be asking but not the specific questions.

And so, we're going to be asking the public in this 60-day comment period to see, look at that abbreviated information and give us comments back on it.

And then we will take that information, we'll put it together into our final package, going to OMB and hopefully getting OMB's approval for us to go out with the final Federal Register.

OMB has 60 days to respond once we put our information together and put in our formal request, they have 60 days to respond.

So, I've got 60 days now for the public to comment; that ends May 4th. It'll take us a little bit of time to take the comments and put them together and prepare the final package. And then OMB has another 60 days after that. So, probably about three months later is where we may be able to publish our Federal Register if everything goes well.

At this point, I'll turn it back to Ashley.

MS. COCKERHAM: Next slide, please?

So, as Donna-Beth just said, we're in this first green bullet here - in the 60 day period for the OMB clearance. It's the publication that they've put out saying ''is this reasonable?''

And we'll do what Donna-Beth mentioned; we'll have the 60 days, 60 days again for them to look at it and then once we actually issue the Federal Register notice that will be out for 60 days for public comments.

And then about the time that that's happening is when we'll also start our workshops. And those workshops will be to collect the information that is requested in the Federal Register notice.

So, those two will be complementary and then we'll have several workshops over several months throughout the country and this year, we're also going to be drafting the website and I know that a draft of the website will go to the ACMUI for review and for input and then before anything is finalized.

So, that's what's going on for this year.

Next slide, please?

And then 2016 and beyond, we'll have, like Donna-Beth said, we split this into two separate things, guidance and rulemaking. We're going to have a second set of workshops for the rulemaking -- for the potential rulemaking to discuss whether or not we should pursue rulemaking.

And after that, we'll collect all of that information, put it in a Commission paper, send it up to the Commission for a vote and they'll tell us whether or not to pursue rulemaking. You guys know how that process goes: proposed rule, final rule.

And we would also be revising the Reg. Guides to complement any rulemaking that's necessary.

Donna-Beth, do you have anything else to add?

DR. HOWE: I think in this point to bring back the research project because one reason that we're looking out so far in 2016 and even out to 2019 is that there's a -- Research has got a project going on patient release and they're collecting data in a totally different perspective.

And their data and our data will come back together potentially for future rulemaking and definitely for the guidance development. So, we're

off on divergent paths and then we'll come back together and that's why it's going to take as long as it's going to.

CHAIR THOMADSEN: Thank you very much.

Questions or comments from the Committee?

Yes, Dr. Mettler?

DR. METTLER: I'm sorry to be a pest.

CHAIR THOMADSEN: That's what you're here for.

DR. METTLER: So, I actually wrote the ICRP document on patient release. And when we were doing that, the thing that impressed me is when I went back to look at some of the scientific underlying issues about guidance and saying, well, just where did this come from?

Like, you have to, I don't know, flush the toilet twice. It's like, really? Did somebody actually ever figure this out? And does it really make any difference?

And I mean I went all the way into figuring out where the sewage went and how much the sewage workers were exposed and did it get into the trout and, you know, so on.

But, one of the things that came up to me

when you start looking into the gory details of this is about the worst thing you could do after you've had radioiodine is to go kiss a baby because of the saliva and the transfer and the uptake in the kids and the sensitivity of the thyroid and all the rest of that.

And that a bunch of the guidelines that are out there are interesting but they have virtually no biological effect. And some of the things that probably have the biggest biological effect somehow don't really seem to get much attention.

At least, you know, you get the whole list of things but not in any order of particular importance.

And so, I always ask, well, that's just like rinse your laundry twice. Well, I mean I try. I went home and looked at my washer, right? It's like, okay, so I run it through and it's done. Now, how the hell do I hit rinse again?

DR. HOWE: You turn the knob around.

DR. METTLER: No, not on the digital computer one, I'm sorry, it doesn't work that way.

DR. HOWE: Extra rinse then.

DR. METTLER: And does that really make

a difference?

But so, I think some of this stuff that's out there, if you're going to put it on a website and make guidelines, somebody better have some underlying data.

DR. HOWE: Dr. Mettler, just to kind of respond on that. The website information is going to be -- we've been directed to make that information more like what does the patient need to know before the treatment? What is I-131? What is the I-131 treatment? What is the preparation?

A lot of things in practice in medicine and all they want us to do is to be able to have a patient go to one site and find links to other sites that will provide them with information. So, that's kind of the focus of the website.

Some of our other guidance, there's a form that's supposed to be a patient licensee acknowledgment form. That's going to -- what does the physician and the patient talk about in order for the licensee make a good determination on when to release the patient.

Because what we're looking at from our study is the patient is the key to radiation safety.

They need to understand what they're getting. They need to understand how they can reduce exposure to others and they need to be able to do things that get reasonable instructions at the end that they can follow. So, that's what we're focusing on this one.

The health physics and the calculations and the actual external dose and internal dose are more the subject for the research study.

DR. METTLER: The thing about links, though, if you link, for example, to the Society of Nuclear Medicine Guidelines, and you just start looking at stuff like, do I need a pregnancy test? Yes or no for x amount of radioiodine.

You get disagreements. So --

DR. HOWE: And we'll have to deal with that when -- well, we'll see because it may be the Commission wants clear and consistent guidance. And the reality is probably not clear, not consistent.

DR. METTLER: Yes, because if you link to some of these sites, you're going to get information that NRC may not agree with or may have different ideas on.

And I'll let you talk about the Society of Nuclear Medicine Guidelines. But, I think there

are issues in there about you can do diagnostic I-131 studies and not have to a pregnancy test or anything.

CHAIR THOMADSEN: Yes, that is a --

MEMBER DILSIZIAN: I mean I was -- you know, I came new to this topic and I was struck how much variability there was among physicians instructing and education of their patients before and after release.

And my role is also a nuclear medicine physician, so I do give I-131. And as I was giving a patient release forms and instructions, I realized that we all have our own, you know, in-house produced forms.

I was wondering, even though there are documents, guidelines for various societies, would it be under the NRC's umbrella to have a uniform [set of] patient release instructions that physicians can at least read and guide patients so it would be much uniform that variability among the university hospitals versus community hospitals? Would that be under our umbrella?

DR. HOWE: That was the gist of the Commission direction that we received was that they were quite concerned about the variability and lack

of clarity. And so that's why they directed us to do what we're going to be doing.

DR. DILSIZIAN: Will we, at the end, have a document that would be uniform? Is that the goal?

DR. HOWE: That is the goal. I don't know whether it is achievable or not. I mean we won't know until we get the information in.

And I think the other thing that I haven't emphasized is that when we go out to collect this information, we are asking for [what's] already existing. We are essentially dependent upon the physicians and the patients to tell us what really works well for you?

And then we'll take that, we aren't asking anybody to develop anything new, we're just saying, physicians, what really works well for you? Let us know, share it.

MS. COCKERHAM: When we issue that Federal Register notice, we would want to see that form. Hey, here's an in-house form that we have that works well for us and if we can see all of those forms, that's the information collection that we want to go out and get.

DR. HOWE: And we'll have very specific

questions. I'm going to have questions that are more oriented towards the medical community and I'm going to have questions that are more oriented towards the patients so that we can get as wide a set of information as we can.

So, I think we're going to try to address those things.

CHAIR THOMADSEN: Yes, Dr. Costello?

MEMBER COSTELLO: I want to comment on patient instruction.

A problem that comes up, and maybe it's unique to Pennsylvania, I don't know, is that Pennsylvania has a lot of radiation detectors at trash transfer stations, landfills and such.

And we get two or three cases a week of them being set off by I-131 patients.

Now, the safety suggestion to that is, they are going to the landfill and they're buried and never bother anybody again.

However, there are some landfills that because of their agreement with their local township or because they incinerate their waste and the township doesn't want radioactive place incinerated for no good technical reason, they're forbidden from

taking radioactive waste.

And so, we got a call from a mother whose daughter has thyroid cancer and whose waste set off their alarms and they were contacted by the company that collects their waste and threatened with thousands of dollars in fines or they would simply no longer collect their waste.

And so, we try to help, you know, we call up the -- and they don't care. You know? And we say this stuff is exempt. This stuff isn't harmful, all the stuff that you would say if you were talking to them, and they don't care.

And we're talking to the mother of the patient who was very angry and she was angry because no one had given her any instructions with regard to what to do with waste. Okay?

I and this patient went to a very prestigious institution in Columbia. But, as you know, all this is not regulated, it's all exempt and there's not much we can do. They want us to somehow or another to punish the medical institution for not sufficiently instructing what to do with the waste.

And to be honest, from a safety point of view, putting patient waste in the trash is probably

the safest thing to do. I'm not sure I want them saving the other I-131 waste and keeping it in wherever who keeps these things.

But, in drafting the guidance, okay, please remember that a lot of this stuff is out in trash. A lot of this stuff sets off alarms and very frequently, the patients, remember our cancer patients, have to be dealing with people threatening to fine them or threatening not to pick up the trash anymore because there was iodine left.

DR. HOWE: And, Frank, you bring out a really good point. We don't regulate the trash facilities, but many trash facilities around the country, they are afraid of radiation so they put in their contracts, no radioactive waste can go to this transfer point, can go to this landfill. And that's an absolute.

MEMBER COSTELLO: We do regulate them, the broader department, and we require them to have detectors. And we issue a lot of DOT exemptions for shipping these things.

DR. HOWE: But we don't license landfills.

MEMBER COSTELLO: I know, we do.

DR. HOWE: Yes. We don't and many landfills do have this because of the local community, no radioactive waste, no medical waste, no whatever waste they consider harmful.

MEMBER COSTELLO: I think it's important that the instruction to the -- the instruction to the patient, at least address this. Since I don't even know what it should say, to be honest. I think throwing it out in the trash is probably the best and safest thing to do, but that mother who had the daughter who had thyroid cancer wasn't seeing things my way.

DR. HOWE: And that's one of the elements that is included in the questions that we'll be going out with.

CHAIR THOMADSEN: Yes, ma'am?

MEMBER WEIL: Many institutions do provide instructions about waste and this just points out the discrepancy of information that patients receive. And it's a wonderful thing that NRC is trying to develop some consistency of guidance for patients in order to address the post-treatment period.

I'd like to make the point that I've made

before; this often we get some push back when we talk about NRC intruding upon the practice of medicine by regulating what kind of guidance patients will receive, what kind of information they will receive about dealing with the post-treatment period.

And I'd like to say that this is not the practice of medicine, this is post-treatment. This is after treatment. This is public health. This is not intruding in any way upon the administration of the iodine; it's simply trying to protect the public and the patient from mundane stuff like never having their trash picked up again and real radiation exposure to infants.

This is different from the practice of medicine.

CHAIR THOMADSEN: Thank you very much.

Dr. Zanzonico?

MEMBER ZANZONICO: Well, that addresses a point I want to bring up.

I thought I heard something to the effect that in this brochure or website among the issues that might be addressed would be side effects, what the patient would expect.

To me, that is now infringing on practice

of medicine. Frankly, I think I'm very leery of a regulator-sponsored website directly conveying information to patients, especially if it now incorporates issues like side effects and this general concept of what to expect.

I mean a physician may decide for very legitimate reasons that side effects that might be considered undesirable might be tolerable under some medical circumstances.

So, how does a patient who accesses such a website and sees some information, reconciles what they see there with what their physician may tell them in a specific case under specific circumstances?

So, I'm just very leery about that component of such a website or brochure or any public outreach.

I feel the most appropriate way would [be to] provide information to physicians and still leave it to the physician to convey that information even with respect to radiation safety practices and dose reduction practices to the physician.

I think it's almost unavoidable that no matter how restrictive the NRC may characterize things, that it's going to start infringing on medical

practice and the patient/physician relationship.

I mean these are not simple issues and I think physicians need to take more responsibility in conveying this information reliably so forth and so on to patients but it's their responsibility. It's not the regulator's responsibility.

DR. HOWE: And I agree with you, Dr. Zanzonico and I think one of the things to keep in mind, the direction that we got from the Commission does take us into practicing medicine but it's done in such a way it's supposed to be a website that the medical community may have a website that addresses a certain issue. And so, we would have a link to that website.

It would not be an NRC requirement. It is just a recognition that patients go up on the Internet and look for things and this would bring some links that would go to professional groups and others that might provide information.

So, we aren't intending to get into the practice of medicine but it looks like it for this website. So, how it turns out, I don't know.

MEMBER ZANZONICO: I think, though, it has to be recognized that just the fact that the NRC

is directing a patient to a website whether they've claimed to have vetted it or not has a certain implication. I mean that's just inevitable.

DR. HOWE: Yes, I appreciate that.

CHAIR THOMADSEN: Ms. Langhorst?

MEMBER LNAGHORST: There's ample precedence for government agencies providing information about drugs and side effects to the public. And this would not be a unique instance.

CHAIR THOMADSEN: Thank you.

Dr. Palestro?

MEMBER PALESTRO: Yes, I certainly agree with Pat Zanzonico's comments and I would express previously my reservations to Donna-Beth. We've even been back and forth on this about establishing a website and providing links.

I think a potential, more than a potential, like a real problem is that you establish these links, you're going to find that some of the websites, you're actually give contradictory information and I think that creates its own set of problems.

And I'm inclined to also agree with Pat, at least if I understand what he was saying correctly,

I think that the NRC should be establishing the regulations and it should be up to the medical community to identify ways to meet them, to satisfy them, not be provided that.

CHAIR THOMADSEN: Thank you, Dr. Palestro.

Dr. Alderson?

VICE CHAIR ALDERSON: I don't disagree with anything that the other speakers have said and I share their concerns.

I just want to make a comment that we've all read in many publications about how patients are using the Internet more and more and more all the time and wise people have described that growing use as disruptive to the practice of medicine.

So, although I share the concerns, I don't think we can ignore the fact that the patients are going to be out there, they're going to be looking at all these things and, in some way, we have some kind of responsibility to be aware of that and to try to respond to it. It's a big problem but it's not going away.

CHAIR THOMADSEN: Thank you, Dr. Alderson.

Can I ask, when would the input from the ACMUI be the most useful in this process? Would it be most useful before you hold the stakeholder meetings? After you get some of the input? When you think it would be efficacious for us to give advice?

DR. HOWE: I think certainly ACMUI members attending the stakeholder meetings would be good. We will be collecting the information from the public and then we will be processing it and we'll be processing into some kind of final product.

And we would be bringing in the ACMUI as we're reviewing those final -- bringing those final products together to finalize them.

So, I think your input should be both in the public meetings and also as we've collected the information, we processed it, we'll be coming back to you with what we find.

CHAIR THOMADSEN: When do you expect that you'd be doing the processing?

DR. HOWE: Well, roughly, if I've got through the 4th of May for people to comment on should NRC be collecting this information and if the burden correct...?

I've got probably about 30 days to

process that information which I think is much more limited and then go back to OMB for the actual request for the clearance. They've got 60 days to act on the request.

So, that kind of puts us into maybe August/September when we would publish the Federal Register asking the public to provide its input on these different questions. And they've got 60 days to comment.

In that 60 day time period while the public is commenting on the actual questions is, I think, when we will be holding our stakeholder meetings.

MS. COCKERHAM: So, later this year.

DR. HOWE: So, it's going to be probably maybe even late summer.

CHAIR THOMADSEN: So, it sounds like we may be would be naming a subcommittee at the next meeting. That nothing would be happening between now and then that we would really be commenting on.

DR. HOWE: I think the next meeting is probably about the right time frame. Things could go a little faster. If they do, we could always --

CHAIR THOMADSEN: Have a telephone

conference.

DR. HOWE: -- have a telephone conference.

CHAIR THOMADSEN: Dr. Ennis?

MEMBER ENNIS: So, I haven't been on the Committee that long, so I want to kind of -- it seems like the core issue here, and my question really is, is this a repeating theme? And, if so, what would I think about it in that way?

What we do with situations where the medical information, scientific information, would suggest we essentially have nonissues and yet, the public or portions of the public want to be more strict than that.

And the tension that exists between our perspective, perhaps, or the scientific community perspective, that it's not an issue.

And the public's anxiety about radioactivity, and this is a recurring theme that maybe we need to be dealing with that more than the particular -- or in addition to at least, or maybe more than the particulars of one particular scenario.

CHAIR THOMADSEN: And, I'll just say that has been an ongoing issue that is precisely what we

do. We always have to deal with those issues. It's not something we can deal with once for and all and say we're done.

It perennially comes up and it's not going to go away because the public has their perceptions, scientists may have theirs. This isn't unique to radiation and both have to be accounted for.

Dr. Mettler?

DR. METTLER: So, one of the things I ran into when I was doing this ICRP thing was all the different countries who are right next to each other had different regulations.

So, the Germans wanted to keep everybody in a hospital for a week and they were collecting all the urine for, you know, I don't know, 30 days and storing it. And the French were just letting them out.

So, all the patients we've got on the train going from Germany to France, getting treated and coming back, end of discussion. I mean that's the whole practice - just went that way.

But, in your -- the two questions I have is, is the collection and processing of this, I know

IAEA has a whole thing out on patient release and are you going to take into account other things like that when you put this all together or are you just going to take the database and then work from the database?

Or are you actually going to try and interact with the other things out there and saying, well, we're going to actually -- this is what IAEA recommends but we're not going to do it because or we're going to something?

The second question I have was, a bunch of us, I don't how many in the room, have gotten calls from people saying there's an RFP out, a Request for Proposals, and I guess there is contracts or grants to find out how many patients are released from each hospital and yadda, yadda, yadda.

So, is that -- that's an NRC thing that there's these groups out there that are collecting information from various institutions and then they're going to feed back to NRC?

DR. HOWE: NRC has two projects going right now. One project is a contract based project that the Office of Research is managing and they're going out and looking at where do patients go after they're released? And what is the expected radiation

dose from those patients when they go to sites other than, say, their home?

So, that may be what you have heard about. That contract is already been let. So, there's a contractor in place and they are working at going through the different steps of the contract and collecting information. And that is separate and distinct from what Ashley and I are talking about.

DR. METTLER: Right, but knowing those things, I assume it's going to take two years.

DR. HOWE: And that's why --

MS. COCKERHAM: And so we are saying they're going to feed that together. Yes, they'll feed back.

DR. HOWE: And that's why we talk about the fact that when we go to guidance, it's going to be several years out because we have to get that information back.

MS. COCKERHAM: To address your first part about the international practices and different things. That was part of the Commission direction and I believe it's Sophie that put that together and it's already gone back up. Was a CA note?

DR. HOWE: I was a CA note.

MS. COCKERHAM: CA note. So, we did do a survey and collected information as voluntary and it was from many other countries and we put that information together and transmit that back to the Commission.

DR. HOWE: One of the Commission questions was, well, how is NRC racking up against the international community?

DR. METTLER: Well, the interesting part of that is when I was doing this ICRP stuff, I looked all around the world and we decided that what the NRC had in place was the most reasonable thing that we could find.

So, the ICRP report is, in fact, essentially based on NRC guidance and we got that through the international community. And it's sort of where the IAEA stuff came out of a lot of it.

And then, Congress came back and said, well, how come you guys aren't up with the ICRP, not knowing that the ICRP basically was using your stuff in the first place.

DR. HOWE: No, we saw a lot of fingerprints on the ICRP. But the equality is that when we went back and collected the international

data there were some countries that had just recently, after the ICRP and way after NRC went to its things, had changed their patient release and they were getting much more conservative. So, they weren't necessarily moving in the NRC direction, they were moving back in the other direction.

So, I think it's a wide open field out there.

CHAIR THOMADSEN: Yes, originally, I had hoped that all the patient release stuff would have been settled while I was on this Committee. Then I was hoping before I retired, but it sounds like now I'm hoping it's done before I die.

DR. HOWE: Yes, you know, it's just 2016-plus on my slide. Like, I'm not even putting a date right now.

MEMBER COSTELLO: And you're still being an optimist.

DR. HOWE: Well, to tell you the truth, I think we're passing 2019 dates.

MS. COCKERHAM: Yes, I was hesitant to even put that on the slide.

CHAIR THOMADSEN: Ashley, your child will take over.

Ms. Dudes?

MS. DUDES: Well, I appreciate the dialogue on this and I think there's a lot of common ground. This is one of those topics where we absolutely need the ACMUI and lock step guiding and directing the staff as we're going through this project.

I'm also very leery about us having a website because, although I did go on a website one day, Donna-Beth gave me a video to watch someone [who] had I-131 treatment.

And then I went on looking for information about what do I do? And I was all over the map. And I thought, well, and I'm not clear that the regulator should be telling the patient about the side effects. But, perhaps, if you could have some fundamental agreed upon guidelines with the experts, that would be very useful. I'm not sure I'd go the NRC necessarily.

I don't know if I'd know to go to the Nuclear Regulatory Commission if I was having an I-131 treatment.

But I think the fundamental is what do you do? It's don't kiss a baby, right? What do you

do with your waste? Keep and make sure that if you're this, that you have enough time before the treatment to make the arrangements that you need to do.

I mean you know, you get a simple procedure done and you're uncomfortable and you're challenged. I mean this is a lot more complicated and you have to take some precautions.

And I like the fact that you're talking about, hey, we should have a standard set of guidance and forms. But ACMUI can tell us that and we don't have to wait until 2019.

I mean it's great to have an endorsement and once we're getting information back from our solicitation, if there's a form that we can get out and say, hey, this is what we think is the right thing. Tell us, because, you know, I worry when we have these multi-year projects that, you know, the staff keeps working and then other life goes on, members change.

And as much early direction as we can get and participation, and I know you talked about a subcommittee at the next meeting and that would be great so that there's an ongoing dialogue and really directive.

I am worried about us being the brochures/website experts. And it's so confusing. But and comments like, keep your website to here's the things you should know post-treatment for public health and safety and other things and for your safety as opposed to here's the impacts of I-131. That should be in the medical journals and such.

So, I mean, so I would encourage everyone to stay very active and communicative and directive and taking positions or the staff. That's what the ACMUI is for.

CHAIR THOMADSEN: Dr. Langhorst?

MEMBER LANGHORST: Whenever we talk patient release, it always comes to I-131. But I just want to remind the Committee that patient release applies to all radiopharmaceuticals, isotopes and so on.

So, that includes Tc-99m, PET scans, Xofigo, microspheres, everything.

So, one guidance does not fit all those situations. So, I know we always come back to I-131, but I just want to remind everyone that aspect of it.

CHAIR THOMADSEN: Dr. Weil? I'm sorry.

MEMBER WEIL: Oh, see, I didn't mean to

catch this. That's not me.

Thank you for that comment because I think it's really important. I mean I recently had a Tc-99 scan and nobody told me not to go near my pregnant daughter. Now, I knew but there should be information about that on a website that's accessible post-treatment for patients who have questions, who may not get the information that they need from their clinician.

CHAIR THOMADSEN: Thank you very much.

Any other comments from the Committee?

Hearing none, thank you very much, Ms. Cockerham, Dr. Howe.

This brings us to patient intervention, which will be Dr. Gabriel and Mr. Costello.

DR. GABRIEL: Good morning.

ACMUI requested to discuss patient intervention at this meeting and I was asked to open the discussion by providing some background information and the history of NRC's use of the term patient intervention.

Next slide, please?

Let's start with NRC's current definition of patient intervention and then go back to trace the

history of this concept.

NRC's medical regulation, 10 CFR Part 35 includes definitions of terms in Section 35.2. This slide shows the current definition of patient intervention and intentional or unintentional actions by the patient such as dislodging or removing treatment devices or prematurely terminating the administration.

Next slide?

The current regulation uses the medical event to describe deviations from intended administrations that need to be reported to the NRC.

The older term, misadministration, was first introduced in 1980. The concept of patient intervention was acknowledged in 1980, although the term was not added to the regulation until 2002.

Next slide?

The requirement to report misadministrations was added to Part 35 in 1980 and after the final rule was published, the NRC received a number of questions from licensees about the definition of misadministration.

In response to these questions, NRC issued a letter with a series of questions and answers

illustrating what constituted a misadministration.

And then, the slide shows a question and answer that may involve the first use of the term patient intervention.

So, the question asked if the misadministration has occurred when the patient stops attending treatment sessions and the total dose is not delivered? And this was in era where cobalt-60 teletherapy was in wider use than it is today. So, that's likely the kind of scenario this question was addressing.

And the response was that patient intervention in the treatment plan is not a misadministration. So, it appears that the term patient intervention pertained to patient behavior that was not under the control of the licensee.

Next slide?

The next major rulemaking was the 1992 Quality Management Rule. The rule did not address patient intervention. Another clarifying letter with sample questions and answers was sent to licensees by this time, there were no examples involving patient intervention.

In documents the NRC files from error

indicate that NRC made determinations of patient intervention on a case-by-case basis. So, there was no public addressing on the concept.

Next slide, please?

The next major proposed rule was issued in 1998 and SOC stands for Statements of Consideration. And the Statements of Consideration for the proposed rule discussed patient intervention as a problem area in misadministration reporting. So, attention is starting to be paid to this.

The terms misadministration and medical event are both used in this document. This was the proposed rule that changed the terminology to medical event.

And this slide includes in the second bullet a quote from the Federal Register notice. It starts with the language licensee is expected to act reasonably in accordance with prevailing standards of care to prevent a medical event.

It continues, in cases where patient intervention is probable, the licensee should take reasonable actions to avoid a medical event such as using extra sutures in the case of a temporary brachytherapy treatment, extra taping or more

frequent checks by nursing staff.

So, it appears that the term patient intervention still pertained to behavioral actions on the part of the patient.

It was also noted in this document that, in some cases, the licensee might be able to anticipate that patient intervention was likely to occur and there might be steps that the licensee could take to prevent the undesired patient behavior.

Next slide, please?

This 1998 proposed rule included language to incorporate the concept of patient intervention. The proposed wording included an exception from reporting for, and I'll quote the phrase, ''administrations resulting from a direct intervention of a patient that could not have reasonably been prevented by the licensee.''

The Federal Register notice for the proposed rule specifically asked for public comment on whether a patient intervention was adequately addressed by proposed changes.

Next slide, please?

The final rule corresponding to the 1998 proposed rule was issued in 2002. The Statements of

Consideration for the final rule stated that the phrase, ''that could have been reasonably prevented by the licensee'' was deleted. The deletion was in response to comments from the public that this phrase was ambiguous, subjective and infringed on the practice of medicine.

The Statements of Consideration also described a new requirement that was added for licensees to report events caused by patient intervention if they resulted in serious consequences.

The description of serious consequences was unintended permanent functional damage as determined by a physician.

Next slide, please?

The same Statements of Consideration also presented the definition of patient intervention, the same one that's in effect today and that I described at the beginning of my presentation that is intentional or unintentional actions by the patient such as dislodging or removing treatment devices or prematurely terminating the administration.

And finally, the Statements of Consideration reiterated the expectation for

licensees to act reasonably to prevent patient intervention that could result in medical events.

Next slide?

The 2002 final rule includes the version of the medical event-reporting requirement 10 CFR 35.3045 that remains in effect today. And Section 35.3045(a) introduces the medical event reporting requirements and excludes reporting of events resulting from patient intervention.

Next slide?

When you move to the next section, 35.3045(b) also mentions patient intervention. It states that under some circumstances, medical events resulting from patient intervention do need to be reported. A report is required if the event resulting from patient intervention results in or is expected to result in unintended permanent functional damage to an organ or physiological system.

The determination of unintended permanent functional damage is to be made by a physician.

Next slide, please?

So, I wanted to provide some examples for this presentation and I searched historical NRC records for formal case reviews that evaluated

whether patient intervention was the cause of a misadministration or medical event.

The most common types of cases that I found were those in which the patient removed a brachytherapy applicator before the conclusion of the treatment of a patient in motion accidently caused an implant ribbon or an applicator to become dislodged.

Many, but not all, of those case reviews concluded that patient intervention was the case of the misadministration or medical event.

However, in some of the cases, a determination was made that while patient intervention may have been a contributing factor, there were reasonable steps the licensee could have taken to avoid the event or react more appropriately when it was identified.

There was one unusual case in which, after administration of an I-131 capsule, the patient surreptitiously removed the capsule and concealed it. The determination was that the patient actions in removing the capsule were consistent with the definition of patient intervention and the reporting exclusion in 25.3405(a) could be used.

Next slide, please?

The most recent communication issued by the NRC about patient information was an Information Notice in 2006 related to gamma stereotactic radiosurgery treatments. Two cases were described in which patient movement caused the head frame to be displaced resulting in dose to an unintended site.

And if you're interested in the details of those two cases, I can refer you to the Information Notice itself.

Next slide?

The Information Notice noted that both licensees believed it was not necessary to report a medical event because they viewed the patient movement as patient intervention.

However, the NRC disagreed and viewed the events as resulting primarily from issues with the patient equipment set up.

The NRC suggested a number of actions that licensees should consider taking to avoid medical events caused by patient intervention for all treatment modalities, not just for gamma stereotactic radiosurgery treatments.

Next slide?

So, finally, as you know, a major Part 35

rulemaking is currently under way and the proposed rule this time did not make any changes regarding patient intervention.

On the slide are some definitions and this concludes my presentation.

MEMBER COSTELLO: Thank you, Sandy.

Bruce, before you start, any questions for Sandy?

CHAIR THOMADSEN: Dr. Mettler?

DR. METTLER: It said that it's when -- it has to be reported when it results in permanent functional damage. How does taking out an applicator result in permanent functional damage?

DR. GABRIEL: That would be an example of a case that likely would not result in permanent functional damage.

DR. METTLER: So, anything that they pull out that's an under exposure is not a misadministration and doesn't need to be reported?

DR. GABRIEL: That's what the rule says, however, considering the case examples, it looks like in a number of cases similar to that that the NRC has formally evaluated. The determination was made that patient intervention was a contributing factor but

not --

DR. METTLER: But see, that's what --

DR. GABRIEL: -- but not the major cause.

MEMBER COSTELLO: Let me interrupt.

I think that precisely if the NRC has determined, I guess, that if the institution could have anticipated that the patient would remove it and taken steps to make that more difficult or unlikely, then it would still be a medical event.

DR. METTLER: But it doesn't -- it said it's a medical event if it causes permanent damage.

MEMBER COSTELLO: I don't think it says that. I think it says even if there is a patient intervention, if it causes medical damage, it's a medical event.

DR. METTLER: If it doesn't?

MEMBER COSTELLO: If it does.

DR. METTLER: It is does? Yes, if it doesn't cause permanent damage.

MEMBER COSTELLO: It could still be a medical event. It meets the definition of a medical event and it doesn't meet the definition of patient intervention.

If there's permanent damage, even if

there is patient intervention, it's still a medical event. But that's pretty rare.

DR. GABRIEL: Thank you for answering that question.

MEMBER COSTELLO: I can't help myself, Sandy.

Did I do okay?

DR. GABRIEL: Yes.

MEMBER COSTELLO: Any other questions for Sandy that you can answer?

Okay. Next slide, please? Oh, let's go back to that slide.

Some of you may recall when we had the subcommittee that was looking into guidance for microspheres, in particular, looking for guidance initially involving shunting to the GI tract then we expanded it somewhat further than that.

There was a lot of discussion amongst our group about patient intervention. So, if the -- basically we came to the conclusion if the treatment put the spheres in the right place but due to the patient's anatomy it went to the wrong place that we would then consider that not to be a medical event. Because what more could the doctor and the medical

team have done?

Well, and I heard that expressed for any of people and we'll get to that later on the slides. Well, as I think most everybody here, I don't know about the audience, knows I worked for the NRC like forever, even when Sandy was there.

And that wasn't my recollection of what the NRC meant by patient intervention, that that was more of a type of passive patient intervention rather than active patient intervention.

And that troubled, because I think that the NRC and its Advisory Committee, it's important that they mean the same thing by words like patient intervention. That we don't have a situation where the ACMUI's advising the NRC in a particular case, let's say. And say, well, that's not a medical event because of patient intervention and we're meaning different things by that phrase.

Now, I'm not advocating a particular definition; I'm not. I want to call this both to the attention of the Committee and to the attention of the NRC so we can become aligned and mean the same thing about the same words.

Okay, go the next slide, please? Thank

you.

The NRC basically has viewed patient intervention as actions by the patient, behavioral actions rather than physiological phenomena, how to put together a pubic arch in an inconvenient place or, you know, vascular systems to go the wrong way or the patient just body is not cooperating so that when the medical team does everything according to their procedures, the outcome is not what was intended.

So, by my past experience was that if the anatomy result and sources coming to the wrong place, that that would not constitute a medical patient intervention.

But it's clear to me that overwhelming the Committee felt that if the doctor did everything right and the team did everything right and sources went to the wrong place, that's not a medical event.

Next slide, please?

So, in preparing for this, is I want to think, how could I express what I heard from the Committee on patient intervention? And thankfully, the Committee told me in many emails and things.

So, if you wrote me on patient intervention, I scoured my emails and I tried to

capture your thoughts because I wanted to accurately reflect what I believe the Committee's thoughts are. Okay?

However, I don't remember whose comments are whose, you know, maybe if you recognize your comment you could raise your hand.

One is there's another case of regulatory terms not being in alignment with connotative and denotative meaning. Basically, what we're recognizing here is, we the NRC, will tell the medical industry or tell people, medical events are not -- they're not violations, you know, they're just medical events.

But I think, and the physicians kind of try, you know, when they hear medical event, they think that they -- it's saying they did something wrong. That's not always the case, I think, from the NRC point of view. But, I think clearly medical practitioners see it that way.

And as this email you sent me, what does actions -- what does intentional or unintentional mean?

Next slide?

I have too many words in this slide, so

I hope you all can read this.

Look at all these various things that can occur within the patient, changing flows so the results that things get, you know, the seeds or the microspheres go to the wrong place. These are -- and it carries all the suboptimal treatment. But again, once again, when the doctor and his team stop the treating part, everything was going fine from their point of view and then a person's body intervened.

Another couple of these occurrences are not the fault of the patient. There's no meaning to saying it's the patient's fault unless the patient gets up and walks off the table or pulls out a tube or something, nor the AU, nor the administering physician or team.

And the question they ask is, what can be done in reporting such things when the person's anatomy causes it? What can be done in the future to avoid medical events? Okay?

Now, I want to remind you what Sandy talked about what the NRC's view of patient intervention. That doesn't capture those type of events.

Next slide, please?

If during the injection of microspheres, the patient's artery contracts and you have microspheres going into the GI tract, the thought of my ACMUI colleague was that, too, would be patient intervention. But I'm telling you I believe that historically, that would not meet the definition of patient intervention as interpreted by the NRC.

I'll repeat, I'm not trying to argue whether that should be patient intervention or not. Okay? I don't know. But, I don't want to have this misalignment between the Committee and the NRC, which maybe that is and then lung shunt fraction and so forth.

Next slide, please?

As I said, the NRC and its Advisory Committee seem to be misaligned on patient intervention. I'm going to go further than that. I think it's even a misalignment on medical events in general. And I think that the Committee basically believes that the doctor did a good job and couldn't have done any better. That's not a medical event.

And I don't believe historically, that the NRC is seeing it that way.

You don't want to have miscommunication

between the Committee and the NRC when we're using the same words that have different meanings behind them.

And the last question is, does whether the Authorized User medical team did something wrong, is that the sole determination of whether there's a medical event?

If the Authorized User and the team did everything according to protocols, should that be considered to be a medical event?

So, I want to have this discussion today, that's the last slide, to call this, I think it's this misalignment to the attention of the Committee and to the attention of the NRC so we can resolve it.

Perhaps we could have a subcommittee to be the committee recommending an interpretation of a medical event of a patient interpretation.

It's a challenge because we're talking about black letter regulation. I mean 35.2, I guess, is the definition of patient intervention. It's there and I don't know if changing guidance can change that.

I'm better on, you know, why's and what's than how's. But I would leave it to the Committee

working with the NRC to come up with a good how to resolve it because I don't think the present situation is a good one.

Thank you.

CHAIR THOMADSEN: Thank you very much.

Comments from the Committee? I'll guess we'll start around the table.

Dr. Ennis?

MEMBER ENNIS: So, kind of more of a general comment but reflecting on this. So, one of my other hats in life I spent a good amount of time scholarly understanding of the development of Jewish law. And if you study the law, any kind of law really applies, words, even when they're black letter, often change meaning over time in the community.

And as long as everyone is in agreement, it works and it's not necessarily a problem.

So, again, I don't know how NRC feels, but the fact that everyone many years ago felt the phrase meant one thing and now everyone feels the phrase means something a little bit more because we've gotten a little more sophisticated medically or we've broadened our understanding, to me, it's not necessarily a problem unless there's some kind of

clash.

MEMBER COSTELLO: Thank you. It's a very good question.

Is there any representative from the OGC here today?

MS. HOUSEMAN: Yes.

MEMBER COSTELLO: Hello. I understand you're new to us.

MS. HOUSEMAN: Yes.

MEMBER COSTELLO: I think congratulations.

From my previous life, okay, such questions often wind up being resolved by attorneys, for better or worse. Okay?

However, I think that the meaning of patient intervention within the NRC, perhaps, has not evolved while the meaning of it in the medical community has and I believe that to other people.

But, I think that's a true statement. I think that, you know, we're going back -- how far did you -- 1992?

DR. GABRIEL: 1980.

MEMBER COSTELLO: 1980. You know, a lot has changed, a lot of modalities have come along. We

weren't talking microspheres in 1980, you're talking, you know, Cobalt and Cesium and gynecological implants or something.

But, it's a lot more complicated now than it was then. And perhaps, perhaps, our understanding of that term should change, but it hasn't changed yet.

And so, right now, if the Committee says, this is not an event because of patient intervention, the NRC understands something fundamentally different.

CHAIR THOMADSEN: Thank you.

MEMBER COSTELLO: A full evolution of.

MEMBER DILSIZIAN: Great discussion.

So, to me, these are the words, patient intervention and the other key words that said behavioral actions, intentional or unintentional.

MEMBER COSTELLO: Right.

MEMBER DILSIZIAN: So, and I understand the evolution. So, if I were to say to you, patient intervention, that is one, instead of putting behavioral actions parenthesis intentional or unintentional.

If we say intentional behavioral, because

behavior is doing something intentional or unintentional action due to anatomy or physiology, I think that would clearer. Isn't it?

MEMBER COSTELLO: If that's what the decision is to do. I mean much clearer.

MEMBER DILSIZIAN: Yes, it's a medical event, but see, the point is --

MEMBER COSTELLO: It'd be clearer but different.

MEMBER DILSIZIAN: Yes.

MEMBER COSTELLO: It'd be clearer but different.

MEMBER DILSIZIAN: Yes.

MEMBER COSTELLO: I'm sure it's unclear now.

MEMBER DILSIZIAN: Yes.

MEMBER COSTELLO: But that might be better.

MEMBER DILSIZIAN: Yes.

CHAIR THOMADSEN: Dr. Weil.

MEMBER WEIL: No.

CHAIR THOMADSEN: Ms. Weil, I'm sorry.

MEMBER WEIL: But I do appreciate the promotion, honorary, whatever.

I think what we -- it's important to know why you're collecting the data before you define the terms that will drive the data.

And it seems to me that there are two different things here that should be captured. One is, is this particularly therapeutic or diagnostic modality creating a lot of medical events that harm patients? Is there a particular practitioner or a group of practitioners that harming the patients?

But the other thing is the one that's unintentional, the one where patient anatomy or patient behavior is the driving factor for the failure, then there's a problem with the therapeutic modality.

And there are different things that you want to collect and we're trying to lump them in one category of medical event which doesn't make sense because they each have meaning and they should be looked at separately.

MEMBER COSTELLO: If I could respond to that.

Medical event, if you look what's supposed to happen when there is medical event, it'll tell you something of the purpose of it.

One thing that's supposed to happen is you're supposed to report it to your regulator and if your regulator's agree it's [a] mistake, like ourselves, we then report to the NRC.

Another thing you'd have to do is you have to tell the referring physician and the patient. Okay? And if the patient, for whatever reasons it's not safe for the patient to tell us, you tell the physician, the family maybe you're looking.

So, these are two different things. You're doing on the wholesale level what you're telling the regulator does. And the regulator can process those. I think with the next speaker we're going to have a review of medical events. Well, we're not going to be focusing as much on the individual events, well, what did we learn from these? You know, what's it tell us about the modality?

So that's doing -- I think it's going to be in the wholesale level. But, we're doing more than that, we're telling the patient and telling the patient isn't for the intention of what did we learn about this modality, it's telling the patient what happened.

And these are very different things. And

a physician can respond to me. I think the concern normally about something being called a medical event when it shouldn't be, let's say, is not so much notifying the regulator, it's talking to the patient who may have had a perfectly good treatment and telling them they didn't have a perfectly good patient.

And, I'll tell you, as a cancer patient myself, the last thing I want to hear [when] I'm treated is that didn't really go right. That helped.

CHAIR THOMADSEN: One comment on the two purposes. One thing about identifying problems in the procedures could come from reporting the incidents to an incident reporting database. They don't have to rise to the level of an event.

Well, that's right, there are reasons why people should want to and there is diminishing reasons why they don't want to. But that's where that data would be better coming from.

Dr. Mettler?

DR. METTLER: Yes, the simple -- I mean this is nothing new. We inject patients with x, they have an allergy. Boom, something is bad. Doctor did everything fine.

Yes, it gets reported, like you said, to a database so the FDA says, so many of these happen and it gets put in the patient chart so nobody injects him with it again.

But if you start going after -- if you just think about where you would go with this as a misadministration kind of bit, there are patients in radiotherapy who are radiosensitive. And you go along and all of a sudden, whoops, they're having a reaction you didn't expect. So, they've got some permanent damage. It's not the doctor's fault.

You're going to report every radiosensitive patient as a misadministration? No.

So, I think you don't want to go there.

MEMBER COSTELLO: Let me pick up on the words you used there and I think is a source of some of this issue, and that's the word fault. Okay?

I believe the NRC, if asked, would say that a medical event can be nobody's fault. It's not medical fault, they're not looking for fault.

DR. METTLER: But if it's due to patient physiology of that particular patient, all you want to do is not do it to that patient again.

MEMBER COSTELLO: My point is the absence

of fault; I think the NRC's point of view is not a reason not to make it a medical event.

However, I think, and correct me, that if I am the physician, the Authorized User, it's all about fault. Okay? I'm having to report this treatment that went badly to the NRC and tell the patient, it goes on the websites and it's made public, I think that somebody's going to think I was at fault. It's only human.

Again, I'm not proposing a solution to this because I don't know. But, what I know is not good is the status quo where the Committee and the NRC look on a very important term, patient intervention, ultimately medical event, you know, why do we report these things differently? And I want us to be in alignment.

What we're going with, I'll leave up to the Committee.

CHAIR THOMADSEN: Thank you for thinking of us.

Other comments?

Not hearing comments, I'd like to name a subcommittee to look into this issue and report back to the whole Committee with a proposed statement of

what we consider a reasonable definition of patient intervention.

And I would ask Dr. Dilsizian to chair the committee, if he's willing. I recommend Dr. Ennis, Mr. Costello, Dr. Suh, Dr. Alderson to sit on that committee and if Ms. Weil would also join that committee, I think that be useful.

Any comments?

Good. Yes?

MS. DUDES: I think that I will get a hook from both sides of my staff when I raise this issue, but so you talk about the common definition of patient intervention. If there's a little discussion, again, it goes back to Ms. Weil's point about what are you doing with the information?

So, we have this phrase, medical event, and it's defined in our procedures. But then there's the usefulness of operating experience that helps you identify trends and other things.

And is there another way to get to that level of detail where there is no fault assigned? But it's still -- because I would agree with Frank that I think that if the staff believes, we like that a medical event, there is no fault, but we use it as

operating experience and trending and, you know, is there things out there that we should be communicating to the broader community?

CHAIR THOMADSEN: And as I said, that was in the presentations we had at the last meeting, discussions of reporting systems that are out there. I think that's pretty much their job. I mean they're completely blameless, so to speak.

And it might be very likely to get more information than what you would get in reporting events, a medical event, according to our definition.

And I would also ask Dr. Gabriel, would you be the staff contact for that? Would that be appropriate?

DR. GABRIEL: I will turn to my boss.

CHAIR THOMADSEN: Since you've already done the research on this.

DR. GABRIEL: Of course.

CHAIR THOMADSEN: Very fine.

Dr. Alderson?

VICE CHAIR ALDERSON: Yes, I have a question that will help Dr. Dilsizian and the rest of us as we go forward.

One of the problems with this whole

discussion, I believe, is that term patient intervention and what that means.

So, in the regulations of the NRC, are we allowed to, among the things, recommend that that term be done away with? Is that within the scope of our recommendations?

MS. DUDES: You can recommend. Whatever the Committee comes to with an independent -- I mean that you are our Advisory Committee. I mean understanding that when we go down that road, that we get into rulemaking space. But I think Part 35, given the evolution of medicine we'll be in a perpetual state of updates. So, absolutely.

How expeditiously we would get that definition change? I don't know, but absolutely. I don't think you should -- this Committee should not feel constrained about what they can recommend to the staff given the expertise there.

CHAIR THOMADSEN: Dr. Langhorst?

MEMBER LANGHORST: As a radiation safety officer who has gone through medical events, from a licensee's point of view, it is an onerous thing to defend to yourself against guilty until proven innocent.

The patient intervention part of it allows the medical licensee to not have to report it to the NRC because the NRC, I understand, medical event to them is an event involving medical application, let's look at it.

But it isn't how we feel on defending ourselves and it's very seldom that the licensee is exonerated.

I've had it happen one time because it's always something about procedures or whatever. And so, you are -- it is a big deal when you have to report a medical event. And you're -- whether it is a medical event or not, it stays on the website forever.

MEMBER COSTELLO: As far as deleting patient intervention, you would have to replace it with something else or you would make it worse because then there'd be no such thing as patient intervention even if the patient does get off the table or pulls out the applicator from HDR, that'd still be a medical event.

So, the definition you're talking about, I think, would capture more of the things we're talking about although, as you know, rulemaking is

very difficult and slow. I don't know how we could treat this in guidance space, I just don't know. But, you know, that's for the Committee and the NRC to figure out.

If rulemaking weren't so hard, we could do a lot of things better, you know?

MS. DUDES: Yes, but there are things we can do in the interim. You know, if there's an agreed upon path forward, I think there's a lot of things that we can do to ease that.

MEMBER LANGHORST: And again, it's that position of what should be regulated and what should be practice of medicine. And there are a lot of things that we, as medical professionals, have to really review when something like this happens with a patient that NRC doesn't necessarily have to be part of.

I mean I think as long as NRC understands that there are other mechanisms that are used to look at what the problem was, how to learn as much as you can from it and minimize it happening for future patients or for that patient, that's a continual thing that changes and I think is worth a look at, too.

MEMBER COSTELLO: And perhaps we need a

rule that says that because that's really -- because we don't have one.

CHAIR THOMADSEN: Well, thank you and -- oh, whoops, we have a comment from Ms. Holiday.

MS. HOLIDAY: I'd just like to confirm on March 19th Dr. Thomadsen formed a subcommittee to review and evaluate the phrase patient intervention.

Dr. Dilsizian has been appointed as the Chair. Additional members include Dr. Ennis, Mr. Costello, Dr. Alderson, Ms. Weil and is that Dr. John Suh or Dr. Sue Langhorst?

CHAIR THOMADSEN: John Suh.

MS. HOLIDAY: Okay, Dr. John Suh and your NRC contact person is Dr. Sandy Gabriel.

Thank you.

CHAIR THOMADSEN: Not that I wouldn't want to invite Dr. Sue Langhorst.

MEMBER LANGHORST: I'm good.

CHAIR THOMADSEN: And if there's no other comments or clarifications, we'll stand adjourned until after lunch at 1:00 we'll resume promptly.

(Whereupon, the above-entitled matter went off the record at 11:39 a.m. and resumed at 1:03 p.m.)

A-F-T-E-R-N-O-O-N S-E-S-S-I-O-N

(1:03 p.m.)

CHAIR THOMADSEN: We'll reconvene, after lunch, and before we start with the agenda, we have a member of the public who wanted to make a comment on the topic earlier in the session, but there was a technical problem apparently with the bridge line at that point.

Are you on the line?

MR. CRANE: I am. And I will identify myself. I'm Peter Crane, retired NRC.

CHAIR THOMADSEN: Very fine. And you want to make comments and you have three minutes, please.

MR. CRANE: Thank you, Dr. Thomadsen. First, my question for Dr. Mettler, when he refers to an ICRP report that he wrote, is that the forthcoming ICRP 128? And if so, is it possible to obtain a copy?

DR. METTLER: No, it's not that report. It was an earlier one.

MR. CRANE: Which report was that?

DR. METTLER: I'd have to look up the number, but it's about release of patients. I can get you a copy.

MR. CRANE: What year was it released?

DR. METTLER: About six years ago.

MR. CRANE: Was that ICRP 94 on doses for patients?

DR. METTLER: I can look it up for you.

MR. CRANE: Okay, well, thank you. What I wanted to say is I wanted to commend the staff for its very conscientious and thorough work in implementing the Commission's SRM. The staff does what the Commission directs in the SRM. I hear some discontent from members of the committee with the SRM, but you know that's out of the staff's hands.

There was a comment from Dr. Howe about how this comes down to the patients. It's all about the patients. I think that's quite right and that's the path down which the Commission went with the rule change of 1997.

Previously, we could -- we, the NRC, could give our directive to licensees over whom we had some control. We're now dealing with the fact that we have transferred a lot of control into the hands of patients, their discretion, their knowledge, their conscience, et cetera. And that puts us in the position of having to educate them.

I agree with Dr. Weil that there is lots of precedence for giving directives to the public, package inserts, CDC guidance, it's all over the place. And I want to say I think the importance of getting guidance out there is underlined by this recent petition for rulemaking filed by Dr. Marcus who is the origin of the patient release rule change of 1997 where she says that fetuses ought to be able to get as much radiation as a worker in a nuclear facility and that it's important to remove these limitations, remove the preferential treatment for women, children, and fetuses. And why do we want to remove the limits on the public so that they can have the hormetic benefits of radiation? So if you have one person out there who believes in ALARA and keeping radiation rates down and another person who thinks that it's beneficial to get radiation and you can see the great, great gap in the kind of guidance that goes out.

And I think that the NRC is doing the right and responsible thing in trying to provide guidance that will be useful to everybody and that has buy-off from the medical community as well. And that concludes what I have to say.

CHAIR THOMADSEN: Well, thank you very much for those comments, Mr. Crane.

MR. CRANE: Thank you, Dr. Thomadsen and members of the Committee.

CHAIR THOMADSEN: And Dr. Mettler?

DR. METTLER: That report was ICRP 94 that was published in 2004.

MR. CRANE: Okay. I have ICRP 94. I'm not sure I read it in quite the same terms you do, although certainly the risk to children from saliva is emphasized in that. Thank you very much and I'll sign off at this point.

CHAIR THOMADSEN: Thank you.

MR. CRANE: Goodbye, thank you.

CHAIR THOMADSEN: Goodbye. Ms. Cockerham, would you like to tell us about 1556.

MS. COCKERHAM: Sure can. Do you want to go to the first slide. I'm sorry some of you can't read this. Sorry it's so small. It's another multi-year project that we've got going on. And so I just kind of wanted to bring you up to date with where we are on revising the guidance. And initially, we had a comment from -- when we did Revision 2 back when we put the NARM rule through, we opened up the volume

and they only made changes for NARM. And during that comment period, we received comments that were not necessarily related to NARM and so those comments were rolled over to be considered now for Revision 3.

So we looked at all of those comments. We also looked at comments received from regulatory staff and the public since the last publication of Revision 2. And we also looked at all of the updated references to know the ICRP, NRCP, all of those documents get updated and so we took a look at all of those to say are we in line with those, can we adopt those as a part of this guidance as well?

So for time line right now, we're in the green box. I sent the document a few weeks ago to the steering committee and so they're looking at all of the changes that have been made and they should be getting back to me here at the end of this month. And then at that time, the document will come to the ACMUI. So you'll see a new version of NUREG-1556, Volume 9, and I have basically a whole list of comments that have been received in an Excel chart and then to the right of it, it says how we've resolved it. And then there are changes throughout the document.

So you're not going to get a redline strikeout because if you did, the entire document would be red. But at least you can see here was the issue, you know, if it's a mobile medical license, and then here's how we resolved it, go see Section 8.4 and then you can go read Section 8.4 to see what changes were made.

So we're trucking along. It's 2015. The top row is the working group that I'm leading and we're in steering committee. Also, our legal counsel is taking a look at the document. And then after the ACMUI has their 60-day review, which I expect they will have in the summer, we'll do a comment resolution, wrap all those comments into the document and actually publish it for public comment, so it will go out again. And we'll do comment resolution again. We'll have tech editing and it will go for final management review and then we'll eventually publish the document.

Now at the same time, we have the Part 35 rule going on, the rulemaking is going. And Donna-Beth has been working on that, Sandy Gabriel as well, and they've been making changes to the guidance, basically in parallel. So they're making changes to

pages. I'm making changes to pages and if you look, the bottom time line is the rulemaking time line. Their guidance went out for comments, so it's already been published. They're ahead of us in that sense. So once they resolve all of their comments and they have final language, I'll take that final language if you look out into 2016 and put that into the document that I'm working on. So we will have one final document at the end. It will all come together, but we're sort of working in parallel on them right now. So I kind of tried to lay out a picture of where we are, where we're trucking along and where we want to be in the end.

So my last slide is just that what I mentioned, the significant changes that actually went into this revision, what were we looking at. I know Dr. Langhorst's name popped up several times. There were letters from her and various NRC staff members, our regional licensing staff, and inspection staff. If they come across things and say hey, could we say this differently or could we say it better in our guidance? Could we be more clear? We made all of those changes.

CHAIR THOMADSEN: Thank you very much.

Comments, questions? Yes, Dr. Zanzonico.

MEMBER ZANZONICO: So the first one is the NUREG revision time line? Did I understand that correctly?

MS. COCKERHAM: They're both revisions to the same document. The first line is the working group that I'm working on which is anything except for rulemaking. So if it's not a rulemaking change -- you know there's changes being made to Part 35 right now. So they need to update the guidance with that. That's being done by a different working group which is the second line. So my working group is on the top time line which was the ''everything else, catch all.''

MEMBER ZANZONICO: Thank you.

CHAIR THOMADSEN: Dr. Langhorst.

MEMBER LANGHORST: And so what you think [is] you may be giving us this summer is that just your group's working on it or will it be everything?

MS. COCKERHAM: Just my group.

MEMBER LANGHORST: Okay. And so then will we see it again when it's all put together or we've already seen it because it went out with the Part 35 proposed rulemaking?

MS. COCKERHAM: You've seen what went out for the Part 35 proposed rulemaking.

MEMBER LANGHORST: Yes.

MS. COCKERHAM: So anything you comment on there will come back to me, the last box on the bottom row where it says final rule and guidance published. Theirs is going to get published and really be a done deal and then I'm going to take any of those changes and wrap it back up into mine.

MEMBER LANGHORST: But it's in the same document?

MS. COCKERHAM: Same documents.

MEMBER LANGHORST: I don't know that I understand that. I'll trust.

MS. COCKERHAM: We have direction from the Commission that when we put out a new rule, we have to have guidance to accompany it. So we have to work with what we have right now.

MEMBER LANGHORST: And I absolutely love that. Thank you so very much. So I'm just trying to figure out what we are going to be looking at what changes may still -- have you already added their changes?

MS. COCKERHAM: No. They'll stay out.

MEMBER LANGHORST: Okay. I think that's very confusing. Sorry.

MS. COCKERHAM: That's why I've created two totally different time lines.

DR. HOWE: This is Dr. Howe. When we have our guidance, you've already seen our guidance once.

MS. COCKERHAM: Right.

DR. HOWE: When we put it in final form, it will come back to the ACMUI for its review and then when it's ready to be actually published, after you have reviewed it and made your comments, we'll resolve whatever comments we have, then it will go out for the public and to Ashley and Ashley will then incorporate it. So you will have a chance to see it, see the Part 35 changes to the guidance, as well as things that Ashley is talking about.

MEMBER LANGHORST: But we will probably see that in two separate iterations.

DR. HOWE: You will definitely see the Part 35 one in a different iteration.

MEMBER LANGHORST: Okay.

MS. COCKERHAM: What we didn't want to do is hold back any work that I could be doing on other

changes, waiting on them to finish all the rule stuff, and so that's why we thought if we did it in parallel, we're making a little more time.

MEMBER LANGHORST: Do you feel like there is anything that you may be working on that's impacted by them, vice versa, in the coordination of the --

MS. COCKERHAM: We've had a couple of little notes and I have just been able to note, like oh, this would be Part 35 rulemaking. We'll make sure we add it to the discussion. So I have them noted.

MEMBER LANGHORST: Okay.

MS. COCKERHAM: No major conflicts.

MEMBER LANGHORST: I think that will be helpful.

CHAIR THOMADSEN: Any other comments?

MEMBER LANGHORST: Just to let everyone know, it is a 512 page document, so I just want to you know.

MS. COCKERHAM: You will be happy to know that it has been condensed down to 300 and some pages.

MEMBER LANGHORST: I like it already.

MS. COCKERHAM: One of my big purposes of this was to sort of change the format, the layout,

how it flows and condense where we can. And so we have taken a big step to do that.

MEMBER LANGHORST: Okay, great. Thank you.

CHAIR THOMADSEN: Any other comments? Hearing none, thank you very much, Ms. Cockerham.

MS. COCKERHAM: Thank you.

CHAIR THOMADSEN: And now we have Dr. Howe with our medical events.

DR. HOWE: Well, good afternoon. This is my yearly presentation on the status of medical events and I will give you all an overview of what we've had reported to us during -- I think it's through Fiscal Year 2014, during Fiscal Year 2014.

And then there will be a working group of the ACMUI who will probably come back in the fall and give its presentation on what it thinks about the medical events. And the two were not supposed to be identical. I give you the overview. I go through in depth on kind of scanning the top of it and we're hoping that in that overview, you'll see some areas that you think you'd like to delve into deeper. And you will eventually -- we will be giving you a copy of the NMED reports that I pulled up. And in those

NMED reports, at the bottom of each event, you'll see references and so ACMUI may want to go into some of those references and try to get additional information or come back and ask the NRC to get additional information. So the intent is not to duplicate things in the spring and in the fall.

First slide. The biggest thing I want you to see here, we have a lot of discussion about medical events and how bad it is for physicians to have medical events and medical licensees. I want you to know that only 46 medical events last year. It's not a big number. It's not a statistically significant number and it's not a big number.

And I always try give you a perspective of where were we last year and this has no statistical significance. It's just to give you just a view. Last year there were about 43 medical events. I've broken it down by modalities so that you can see where things shift from year to year. We very rarely ever get a diagnostic nuclear medicine medical event. And why is that? That's because when we introduced -- either the radiopharmacy rule or the quality management rule, we changed the definition of medical event. For diagnostic, we put a threshold of 5 rem

whole body, 50 rem to an organ. Very few diagnostic procedures will trip that threshold. So we have very few, maybe once every two or three years and we generally have the same diagnostic medical event each time.

And you'll see the 300s, pretty much the same. We had a decrease in 400s. We have much fewer prostate brachytherapy medical events this year. Six hundred stayed about the same, but the distribution changed a little. And the largest numbers are always in 35.1000 because that's where the ytrium-90 microspheres are and that is a very difficult procedure to give in accordance with a written directive because of the mechanics of the device.

So if I can have the next slide?

To put it in perspective, we really don't have anything that you compare on the diagnostic events because even though the denominator is very, very tall, the threshold is very, very high, so we expect to see maybe one every two or three years.

We have about 150,000 therapeutic procedures. We had 45 this past year. That's 1 in 3,000. We've always been told that roughly the percent of human error is about 1 times 10^{-4}, which is

1 1 in 10,000, so it's right in the human error realm.
2 Next slide.
3 So now we'll start going through the
4 different modalities. 35.200 are our diagnostic
5 nuclear medicine procedures. Things that do not
6 require a written directive, so these are all your
7 cardiac scans, your technetium scans, etcetera.
8 Generally, if we have a medical event in 35.200, it's
9 because somebody eluded the generator and gave the
10 entire generator elution to one patient or in this
11 particular case, they had a multi-dose vial and they
12 gave the whole vial to one patient. And by giving
13 them 140 millicuries instead of 20 millicuries, they
14 got a whole body dose of 6 to 7 centigray. So this
15 is what we normally expect to see when have a
16 diagnostic medical event. We don't have one very
17 often. Generally, they are on weekends or at night
18 when you've got multi-dose vials or generator
19 elution.
20 Next slide.
21 I've got three -- we normally call them
22 therapy nuclear medicine, but because you've got the
23 diagnostic whole body I-131 scans in here, we just
24 call it unsealed material, requiring a written

directive. And we've got three of them. Normally, they're all I-131. We have quite a bit of variety this time. We have a samarium one in which they -- this may be one that I want to go back and look a little harder at because the description was that they gave it in the skin as opposed to intravenous and that could be because they missed the vein and therefore it went under the skin or it could be they deliberately tried to deliver into the skin or the arm or somewhere. So I'll have to go back and see, because if it was they missed the vein, we've already made a determination those are not medical events. But I'll have to go back and check on that.

The radium-223, that was a comedy of errors. It was where one error gets promulgated and another error is made and the end result is the patient gets exactly what the patient should have gotten. The hospital has its written directives, written out primarily in millicuries and so when they went to give the radium-223 because radium-223 is given primarily in microcuries, they wrote the number for microcuries, but they put it in a block that had millicuries. And so the written directive is for millicuries. What was administered was the correct

dosage in microcuries. So that's two errors make a right. So that was not one with any significance other than procedures are now being changed so that they are very aware that when they see radium-223, they're going to have to use a different form that has microcuries so the written directive does correspond with what's given.

Next slide.

We have our I-131 patient. This was probably one of our more interesting medical events. A patient came in. They gave the patient the wrong identification bracelet. The patient wasn't supposed to get I-131. They moved the patient along, gave the administration and then the authorized user had not bothered to identify the patient by any other means. So this is a clear example of where they're programmed to ensure the patient gets what they are supposed to get failed in multiple areas. And it's human factors 1 and 2. So that was -- and the end result was this patient got 728 centigray to the thyroid.

Next slide.

These are our sealed source manual brachytherapy medical events. We normally [get] a few gynecological ones and most of them are prostate.

MEMBER COSTELLO: Going back to that, what was the consequence to the patient?

DR. HOWE: They said the consequence -- they didn't --

MEMBER COSTELLO: It just looked like a big dose is all.

DR. HOWE: It's a big dose.

MEMBER COSTELLO: That would be hypothyroid.

DR. HOWE: Yes, there are going to be effects.

MEMBER COSTELLO: Thank you.

DR. HOWE: So we have one gynecological one and we have four prostates. So this is four medical events in 35.400 - is a pretty low number.

So let's go to the next slide.

This is a case where the applicator became dislodged during the treatment. The treatment should have lasted the 63 hours. They believe the applicator was dislodged at 49 hours. The inner thigh received a higher dose than it was supposed to be received. To be a medical event, it has to be over 50 rem or 50 centigray, certainly that. It has to be over 50 percent of what it should have gotten and in

this case it is. So this is the medical event.

Next slide.

So prostate brachytherapy. We're always going to have prostate brachytherapy medical events. One reason we probably will always have it is there is confusion in ordering air kerma units when they need millicurie or ordering millicurie when they need air kerma. So this is one that we've seen before. They've ordered in the wrong units. So you ordered millicuries instead of air kerma.

The second prostate brachytherapy medical event was when some of the seeds were inadvertently implanted into scar tissue and therefore the prostate didn't receive the full dose that it was supposed to receive.

Next slide.

Then we have the ultrasound issues. We're almost always going to have medical events because of this reason. People, the physicians, and the urologists, and the oncologists don't necessarily see the prostate. They see another anatomical area, generally the penile bulb. They insert all of the seeds and it's not until they take an image later that they find they were not in the right location.

So you can pretty much tell these because they're always about 2.5 to 3.5 centimeters from where the target tissue should have been. So both of those were due to ultrasound issues.

Next slide.

Now we've got the 35.600. We had both HDR and Gamma Knife this time. I had a difficult time trying to break down the HDRs for you. First of all, there were a number of different target areas that were being treated, but also there were a number of different reasons for the errors. So in this particular slide, you'll see the different target areas. They had scanned a bronchial, one not designated. It was probably pelvic. It was one designated pelvic and then three OBGYN cases and then we have one Gamma Knife.

So the next slide shows the reason for the errors. Wrong site, wrong patient, decay correction, right patient, wrong treatment plan, source retraction, wrong dwell time, wrong interpretation of dose per fraction. Some of these are common human errors that we've seen many times before.

So let's take a look at the wrong site

ones. We had an OBGYN case where for three of the treatments they gave 700 centigray per fraction and they realized that they had given the treatment later. They realized they had given it 10 centimeters short of the intended treatment site, so they ended up with radiation burns to the patient's thigh and labia. So that one had medical consequences.

The next slide was a bronchial and in this case they had two different segments. One segment used a simple catheter. The other used a centering catheter. One of the segments wasn't delivered correctly. So they discovered the error in the first fraction so they gave the second treatment, which I think is the center catheter was nine centimeters from where it should have been delivered.

Next slide.

We have another OBGYN. They had three fractions and when they checked to make sure the positioning of the vaginal cylinder on the first fraction, they realized that it wasn't where they thought it should be. They attributed that to special patient anatomy, something that you guys would have called patient intervention.

However, when they went to give the

second fraction and they checked the x-ray, they found out it went exactly where they thought it have gone on the first time. So they had an error in the first delivery and they were able to deliver the next fractions the way they were intended in the written directive. So in the first one they delivered 900 centigray to the wrong treatment site. And so it really wasn't patient intervention. It was positioning issues.

On the next slide, this is where we have the wrong patient. And this one was to the skin. They were looking at the correct site. They were looking at the right applicator, but they used the wrong patient's treatment plan. So they delivered the wrong dose to the wrong place. And the area adjacent to where the dose was got about 2,300 centigray to a single point. We don't normally see where they use the right target, the right applicator, but they use the wrong treatment plan. So that one is a little bit different from what we normally see.

The next slide.

This one is a little hard to explain. For some reason, they believed that they needed to put a decay correction for the source into the HDR

treatment plan and did not realize that the HDR treatment plan already accounted for decay correction. Therefore, they had doubled decay correction and they gave too much radiation because the time window was much longer than it should have been. I think this is about the first one I've ever seen that's been this. It kind of sounds like somebody was not familiar with the treatment plans or a new physicist. I don't know exactly why.

The next slide.

We have another wrong treatment plan. In this case they've got the right patient. The patient had two different fractions, but the fractions were slightly different and so when the patient came back for the second fraction they used the treatment plan for the first fraction. And so that put it in the wrong place. And they received about 700 centigray or 60 percent of the dose went to the planned volume.

Next slide.

In this particular case, they had started the procedure. They went to the first dwell location. When they went to the second dwell location, they experienced a resistance and the HDR did exactly what it was supposed to do. It retracted. It would not

go back out. So they tried new tubes. That didn't work. The dummy wire source wouldn't transverse, so they had to abandon this particular procedure.

Next slide.

And this is where we have a dwell time. And they didn't specify where this particular treatment site was. So before the third of six fractions, they realized that for two of the fractions, they hadn't used the correct dwell position. And they didn't give us a lot more information than this. So the corrective action was that they were now going to check the catheter measurements and do a checklist. So you get the feeling that they put the wrong catheter in. That's why they had the wrong dwell times and that was the reason for the medical event.

Next slide.

Okay, this one we've seen, this type of event happen before. You've got three fractions of 500 centigray each. And when they set up the treatment plan instead of saying 3 times 500, they divide 500 by 3. And so the patient got much less than they were supposed to get because they did the fractions, the dose delivered on each fraction was

too low.

Next slide.

This was a Gamma Knife. This was pretty interesting. They had two patients coming. The first patient was going to be a very long treatment. The second patient was not going to be quite as long. They were similar. They put the head frames on. They decided not to treat the long treatment patient. So that meant the first patient that should have been treated was not getting treated that day. But they didn't communicate that information to the nurses. And so when they went to do the treatment, they got the wrong patient and so they gave the patient the second patient's treatment. So they realized they made a mistake about two minutes into the treatment and they stopped the treatment. So it was for the wrong treatment site.

Now next slide.

Now we get to 35.1000. And if you remember correctly, there are 46 medical events total. Over half of them are in 35.1000. The majority of them in 35.1000 are in the yttrium-90 microspheres. What's interesting on the 35.1000 medical events this time is that we did have a

Perfexion and a seed localization medical event.

So if we go to the first slide, so this is another human error. There should have been a clear written directive. The person that was doing -- the treatment planner, knew the patient. Knew the patient had problems on the right side. Somehow did not see the doctor's instructions that this was to be treated on the left side and went ahead and set it up on the right side. And they were -- luckily they caught it about 1.7 minutes into a 19-minute treatment and they realized it was on the wrong side. And approximately 1800 centigray was given for the wrong treatment site.

The next slide.

The seed localization. This is supposed to be a diagnostic procedure. In this case, the licensee received two seeds. They had two markers. One marker was for a benign biopsy. They had two seeds, so they put one seed in the benign biopsy site and they put one seed in the cancer site. So that was unintended dose that was for two days' duration until they explanted the seed and so they received 61 centigray to a half centimeter volume.

The next slide.

Now we'll start with the microspheres. Sometimes we have more SirSpheres medical events. Sometimes we have more TheraSpheres medical events. This time it was SirSpheres treatment. So SirSpheres, we got 15 medical events. They are wrong site, written directive problems, three-way stopcock, bubbles, contamination, transfer error, occluded/kinked catheters, that's normally why we see problems, so there are six of those. It's the largest group. Or no information at all provided.

So let's start. The first one is the duodenal ulcer. In the first of three treatments, they discovered a duodenal lesion and the ulcer developed, it seems to be as a result of the microspheres migrating to the stomach. They did a biopsy. They picked up the microspheres in the site of the ulcer. And they attributed it to aberrant hepatic arterial vasculation supplying the stomach. So that's one of our shunting types of errors.

The second one was in the gastric fundus. They prescribed microspheres to the right lobe. They stopped when they identified unexpected shunting and they delivered a little over 1,000 rads to the gastric fundus.

Our next event, this was an overdose of 13,000 centigray or rads. This is a 10,000 centigray or rads to the lung. In this case, the -- no, have I got the right one? No. Okay. Sorry about that.

This is one where the authorized user provided the radiopharmacist with an incorrect version of the written directive. The pharmacist filled it. They didn't recognize the problem. And they attributed it to failure to follow all procedures and that they had defeated normal checks and balances that would have identified the incorrect dosage. So that was a dosage error. We very rarely see a dosage error like this.

Next slide.

I think from here on we'll see under doses. The first one was a 45 percent under dose where most of the yttrium stayed in and around a three-way stopcock. They sent it back to the manufacturer and they determined the three-way stopcock was defective. So that was a defective device.

The next one, the microspheres were in the tubing near the stopcock valve, but in that case, the device was not defective, but the spheres got

held up at the valve. And their solution was to use dextrose and not saline for the flushing. We hadn't heard that one before.

The next slide. Seventy-five percent under dose. The technologist noticed bubbles in the administration line and stopped the procedure.

The next one is 44. They had elevated readings in the catheter vial interface and they saw coagulation of microspheres. And in this case they actually had contamination of the physician's gloves and the table. So they had more than just the spheres sticking in one place.

The next slide.

Thirty-four percent. There was an error in transferring the microspheres from the delivery vial which was shipped in to the dosing vial.

The next one is larger than expected among of microspheres remained in the needle and didn't reach the patient.

And the next slide.

You had two different under doses. You had a split dose. Each one of them had its own written directive and they didn't realize until they got to the very end that there was blockage in the

delivery system and that neither one of the procedures received the microspheres that they should have received.

The next dose, the catheter was clogged halfway through the procedure. They removed it. They replaced it. And then they were able to deliver the remaining administration, but they lost a significant amount into the catheter.

Next one.

We have an under dose. They were delivering to the same lobe but through two different arterial pathways. And they never managed to get the microspheres through the second part. They looked at it. They had a short arterial segment. They had an acute angle and as a result they had kinking and folding of the tube.

Next slide. They had blockage. They determined it wasn't a problem with the administration kit, but that they had significant kinks, bends, and clots and other blockages at the catheter tip and then they had a 32 percent under dose where the bolus just couldn't be pushed through. And they didn't provide additional information.

And then the last one for the SirSpheres

was a 38 percent under dose, but there was no information provided as to why they believe they had 38 percent under dose.

So the next one is the TheraSpheres. There were nine TheraSphere medical events, two to the wrong site, one reflux of precipitation out, one dose error, one remained in the vial, one settled out of kink.

In the first slide, we have a shunting issue. There were two tumors on the right and the left lobes. They tested for shunting with the right hepatic artery, but they didn't test for shunting on the left hepatic artery. The lobe that they treated was the left hepatic artery and there was more shunting from the left hepatic artery than there was from the right for a factor of ten. So they had expected to receive 370 centigray to the lung. They received 3,450 centigray to the lung and this patient died five months later and the cause of death was acute respiratory distress syndrome.

Next slide.

In this case, they couldn't properly position the catheter into Segment IV. But they went ahead and delivered it and when they did deliver the

dose, very little went into Segment IV. About half of the dose went to Segment IV and the other half went to the right lobe.

Next slide.

We had a reflux and precipitation out where it was 24 percent under dose. There was reduced flow rate during the administration and I think that caused the precipitation of microspheres along the outflow tube.

Next slide.

They were 20 percent under the written directive. They reviewed the treatment plan, but in this particular case, there was a change in the written directive from a normal treatment plan to one where they wanted less activity. So when they reviewed the treatment plan, they didn't verify that the standard activity was not what was being prescribed.

Next slide.

So in this case, 20 percent remained in the vial. Didn't get into the tubing. The one below it, 44 percent under dose. The targeting vessel was flowing slowly. The microspheres settled out prior to reaching the target. The 73 percent under dose,

they had the wrong catheter and they had kinking. We had a lot of cases where they identified a particular catheter brand as having issues for multiple licensees. I didn't bring that with the catheter brand before the ACMUI because we don't know that there aren't other catheters out that they just didn't name the brand on. But this was one of those.

Twenty-three percent under on the next slide. The microspheres adhered to the connector one inch, in the first inch of the manufacturer's supplied tubing. The next one, there was kinking in the delivery catheter. It created blockage. They got a thinner, more flexible catheter walls and small, internal catheter diameter were the contributing factors. So I think we're getting to the point where they're pushing the edge of the envelope and ending up with more catheter issues than anything else.

My last slide is a GliaSite. Probably we'll have to do a little bit more checking on this one to make sure that it is a medical event. In this particular case, the balloon didn't inflate correctly because they put a three-way stopcock on that they were not supposed to use. It's not part of the GliaSite packet. And they put the stopcock on the

wrong position and so the ion tracks didn't go into the balloon to load the balloon up. So we have to check. This may or may not be a medical event depending on whether the patient received the dose. If they didn't receive a dose, then it won't be a medical event, but we don't know exactly where the syringe was in relationship to the patient. So it could have been close enough to give a dose, but the wrong treatment site.

So that is the conclusion of the medical events. We had a wide variety of them. Some of the causes and root causes were things we've seen before.

CHAIR THOMADSEN: Thank you very much, Dr. Howe. Comments and questions from the committee? Questions? Yes, Dr. Zanzonico.

MEMBER ZANZONICO: Inevitably, these kind of self-reporting systems under estimate the actual incidents in this case of medical events. I know it's an unfair question, but do you have any sense of what percentage of medical events are actually being reported? In other words, what is the under reporting rate?

DR. HOWE: I don't think we have a sense of that. We do inspections. Some of the medical

events that are identified come up as a result of inspection because the inspectors, although they're not specifically going to say where are the medical events you didn't report, that comes up in the discussion of how your program is doing. And so we have identified a number of medical events that were not identified by the licensee. And that happens every year.

MEMBER ZANZONICO: But I presume it's not a huge excess?

DR. HOWE: It's not a huge number at all.

CHAIR THOMADSEN: Yes, Dr. O'Hara.

MEMBER O'HARA: The medical event that would involve the remote after-loader where the source wasn't doing -- it wasn't moving in and out as it should, was it ever determined was that a device failure?

DR. HOWE: I think they figured out that there was a kink in the catheter going out and that the HDR device did what it was supposed to do. It could not send the source out so it retracted it. And when they tried the same thing with the dummy source, it wouldn't go out either so it retracted. So it was in that connector going into the patient

where the problem was located.

MEMBER O'HARA: Thank you.

CHAIR THOMADSEN: Yes, Dr. Mettler.

DR. METTLER: You alluded that there might be a problem with a catheter from a vendor, a particular manufacturer. Is there some way that your information on such things gets to the FDA?

DR. HOWE: Yes. We have an NRC-FDA MOU and we can share that information freely with the FDA and we also have certain people in the FDA that have access to our database.

DR. METTLER: So that routinely happens.

DR. HOWE: I haven't shared this particular one, but I can send information over. That's a good point.

CHAIR THOMADSEN: And is it clear that those catheters do get bent in the patient as the patient moves around? No. It's not clear. Dr. Langhorst.

MEMBER LANGHORST: Dr. Howe, do you have a sense of how many of these reported medical events are through Agreement States rather than NRC?

DR. HOWE: That is data that I could obtain, but it is not one that I focus on.

MEMBER LANGHORST: I think it's important to note that when you say that you don't know some of the information, sometimes it's not reported by the Agreement State as opposed to by the licensee. And also do all Agreement States report their events to the NMED database?

DR. HOWE: All Agreement States report their medical events to the NRC and they get into the NMED database.

CHAIR THOMADSEN: Or at least they're supposed to.

MS. DUDES: And that's where I was at. I actually thank the Committee because both of you asked the questions that I was going to pose back to the Committee.

I can tell you that the majority of events that we get are from Agreement States. And that's just a numbers issue. They have the majority of the licensees. And so as we're preparing for our annual action review meeting and you look at the abnormal occurrences that we report to Congress, all of those events come from Agreement States. We encourage and they're supposed to put the data into NMED.

We use our IMPEP process to audit the

programs to assure that they're trying to put those things into NMED and report, make the reports.

We have been trying to do some webinars and training for Agreement State inspectors and NRC inspectors on when you're out how do you look for medical events and it's not necessarily that you're out there looking for the event, but how would you spot one? Because I don't think that's -- it's a more studied type of skill.

Each year we do report to our Commission, okay, here is the status of the program. Here is the number of events. I always feel a little odd in that I don't have a sense of okay, 45 out of 150,000 therapeutic and then God knows how many diagnostic which I think the threshold there, that's a little different. But I was going to pose to the Committee who practices and sees, is this -- would you expect this? But you were asking us the question, so I'm curious what others think because the Commission and I, in my reporting, well, 45 out of 150,000.

CHAIR THOMADSEN: Mr. Costello.

MEMBER COSTELLO: A couple of years ago, I gave a talk at OAS and it was about microspheres medical events and I broke them down by State. I did

this because we had so many. And some States that are huge, perhaps the biggest State, starts with a C, had fewer, had similar events as Idaho.

To get events reported, my view, it's not for us to find them on inspections. It's a very hard thing for us to do. To rely on us finding them on inspections is really not realistic.

MS. DUDES: Right.

MEMBER COSTELLO: What I do ask for inspections, I ask licensees, well, how did they know this was a medical event? You know, is that something, do they evaluate their treatments? Do they think about it? Because if they're not being noticed by the licensees, the chances are they're not going to be noticed. I mean think of the events that are described up there. By and large, inspectors aren't going to find those. Licensees have to notice those.

And so at least -- I know it was in Pennsylvania, I encouraged people just ask a simple question. If trained in modality, just pick a modality. If you had a medical event, how would you know it? And sometimes you get very good answers. Sometimes not as good. I think the best a regulator

can do is to remind a licensee that it's a licensee's responsibility to report medical events because we the States are really not well positioned to identify them ourselves.

CHAIR THOMADSEN: Thank you. Dr. Mettler.

DR. METTLER: The IAEA has struggled with your question for a long time, especially about radiation therapies, and everything else. And I think in general, most people feel that accident reports are somewhere between 10 and 30 percent of what's actually happening, especially since they generally have to be self-reported.

DR. HOWE: And I think Laura brought up a point and Frank brought up an excellent point. If the licensee doesn't recognize it, then it's going to be more difficult to report. Every once in a while, and he's right, the inspectors aren't there to identify unidentified medical events, but as they're asking questions they may trigger something in the licensee that they remember.

I've also gone through a number of years and looked at the Agreement State response. And many times when I'm going through this all of a sudden I

will see a huge number of medical events from a given State. I know that State just had an IMPEP, and so they were asked well, how are your medical events doing? And then they look and either they received them and they didn't pass them on or for some other reason. So we tend to -- and that's one reason that I always present the medical event talk as to what was recorded in the fiscal year, not what happened in the fiscal year because that way if I've got medical events that were identified late, they're going to be captured. If the State is late in getting them in, they're going to be captured. So it gives you the most complete picture by identifying those things reported in that particular year.

CHAIR THOMADSEN: Dr. Zanzonico.

MEMBER ZANZONICO: Just to address your question, I'm Chairman of the Radiation Committee at Memorial, which presumably sees all of the medical events. And we like to think we're very self-critical in terms of what constitutes a report on medical event. And I would say across all modalities, no more than one to two a year with many years having none. And that's a very large number of procedures across modalities. So I think it's at least

qualitatively consistent with a very low ME rate that's reported here.

CHAIR THOMADSEN: Dr. Weil.

MEMBER WEIL: It's fine.

CHAIR THOMADSEN: I think we're going to have to live with that one.

MEMBER WEIL: Just two points, one in response to Dr. Zanzonico, but you're at Memorial.

MEMBER ZANZONICO: Yes.

MEMBER WEIL: Okay, so enough said there. I wonder if there's any transparency or coordination among other entities that collect this kind of data like CMS and State health departments in terms of what get called different things by different agencies. In this instance, medical events, medical errors or unanticipated outcomes. Do you know? CMS collects a bunch of stuff about unusual occurrences. And NRC is collecting stuff. Is there any coordination between those two entities?

DR. HOWE: I don't believe we have any coordination between the two. In many cases, it's because our definition is pretty well defined and it's here and their definition may be something else than over there. We do communicate back and forth

with FDA. If they see something that they think we need to know about, they let us know. If we see something we think they need to know about, we let them know. So we do have that coordination going.

CHAIR THOMADSEN: Dr. Langhorst.

MEMBER LANGHORST: I think last year when we were talking about the various groups that are trying to gather these types of information and near misses and so on, that there was a move maybe to make some of the NMED data public. Is there -- what's the status of that? Because again, it's always good to learn from others' errors.

MR. BOLLOCK: We evaluated that at a public meeting and did quite a bit of outreach and there was not a lot of interest.

MEMBER LANGHORST: Okay.

MR. BOLLOCK: From the public for that.

MEMBER LANGHORST: Okay.

MR. BOLLOCK: It was -- so we made a decision based upon the fact that there are publicly-available yearly reports that give the numbers, the statistics that are available from NMED and there are other ways if you have questions on that, you can reach out to us or the states for specific questions,

but we felt that that was enough.

MEMBER LANGHORST: Okay.

CHAIR THOMADSEN: Mr. Costello.

MEMBER COSTELLO: Two points. One on the public NMED. I think it would be fair to say that because of public NMED there is very open hostility from Agreement States on public NMED. More than disinterest. I can talk to anybody who was talking about that, but there are reasons why the States are not crazy about that idea.

And the second about medical events, at least in our State, they generally are reported on the better institutions. The better institutions, the stronger programs are more likely to identify medical events. Okay? That doesn't mean, I don't think that they have more of them. In fact, being aware of the program, I think they'd like to have less of them, but in fact, they're the ones who report them fairly religiously. Other places, during inspections I ask, might be less likely to do it than the really strong programs.

CHAIR THOMADSEN: Dr. O'Hara.

MEMBER O'HARA: The medical device-reporting database, it's called MAUDE, if any of you

have ever looked at it, it's public. Part of it is public. It doesn't contain proprietary information on specifics about the products. It's undergoing some changes right now. They're changing how it operates. They're going to change the searching abilities of it. And it's gone through a few name changes, too. At one point in time it was going to be called ISIS, but one of the biggest things that has to do with radiological devices is that all of the medical device reporting comes into the same division, the Division of Radiological Health. It doesn't sound like a big change, but it is because the Division of Radiological Health clears or approves devices for the market. And now the same group that clears or approves devices for the market now gets the medical device reports and does the compliance activities with device sponsors. And that's only been a relatively recent occurrence about two years. So there are some changes that are going on with that. Just thought I would --

CHAIR THOMADSEN: Thank you. Comments or questions for the committee? Dr. Suh?

MEMBER SUH: In terms of the medical events, do you sense that the human errors are the

same human errors year after year after year? We're hearing common themes of wrong dose, wrong site, wrong patient which in my mind these should be really never events. If you do the proper time out or are properly trained, the authorized user takes the time to visualize what's going on, is present, that shouldn't occur.

And one of the things I just noticed is that you kind of hear the same story over and over. I don't think it's necessarily the purview of the NRC to just go and regulate medicine, but somehow I think if physicians and others are educated on what's going on, perhaps it will increase the awareness. I can tell you, just being on the committee, it's definitely opened my eyes in terms of how a patient can be seen at a radiation oncology department. So we have really increased kind of our right versus right, identifying correct patient, making sure we electronically document time outs for every single patient because we want to really minimize any of these occurrences from occurring.

DR. HOWE: I'll tell you that back in the 1980s when we brought in the misadministration rule which is the precursor to the medical event rule in

1980, they decided that they would try to do something to reduce the number of misadministrations and they would do it two prong. NRC would do a two-prong approach. One would be rulemaking to capture simple human errors and how can we prevent some of the more common simple human errors.

And the second part would be to go after quality control of devices and so what they found was probably 90 percent of the medical events are simple human error. And we had a rule that was implemented in 1992 called the quality management rule. Many core parts of that rule are still in the regulations and they found out that the most simple human errors that attributed to most of the medical events were identifying the patient. So we had a requirement to use two different methods to identify the patient.

In 2002, we dropped back on the prescriptive nature of that and you just have to identify the patient. The second was the written directive because there were many, many things coming across on the telephone that weren't being recorded correctly. So we went to a written directive. And so those two things. And you will have heard a common thread in here where some people were not looking at

the written directive. The one doing the treatment plan for the Gamma Knife knew or the Perfexion, knew the patient always got treated on the right side and went and set it up for the right and didn't bother to look at what the physician wrote.

So you're right. A lot of these are the same type of human errors, happening in different locations because they are in some respects the easiest human errors to make and it's really difficult to eliminate them, but we try with a written directive and we also tried with the patient identification.

And now, we are adding in the new proposed 35 requirement to evaluate administrations to make sure you don't have medical events. So we're trying to get to those issues. So I don't think I was helpful, but I'm just trying to tell you, we've recognized that was an issue all along and continues to be an issue.

MEMBER SUH: It's just you see common themes.

DR. HOWE: Yes. And it's frustrating because we see the same thing happening over and over.

CHAIR THOMADSEN: Mr. Costello.

MEMBER COSTELLO: Another thing I'll say,

there's a course that they give called the root cause course for investigating. One of the things you learned is be skeptical when human error is always given as the reason because sometimes a little probing, you can find out why the human error occurred. It could be a training issue. It could be a procedure issue. It could be a working condition issue.

It could be a lot of things, but the easiest thing is the patient, if you're an inspector looking into it is say well, the person identified was the wrong patient; it must have been a human error. Well, maybe, but maybe a little deeper looking into what happened you can find out the person had worked so many hours, tired, or the person who was doing the job hadn't got trained or the procedures were bad. Sometimes human error is just sort of a quick, glib answer that the inspector can take and be done and write up the report. I'm just saying, as an inspector, if you spend some more time interviewing people and interviewing the person who made the error, you might find out that there are deeper causes.

DR. HOWE: Also, another thing I would point out in the root cause is many of the accepted

changes are training, but in fact, if you really looked at the human error it's more than training.

CHAIR THOMADSEN: And from human error analysis, you almost always find that there's never a root cause. There's always multiple root causes of these things. You're absolutely right, training is not a particularly effective treatment for these problems.

Other comments from the committee? In that case, thank you very much.

DR. HOWE: Thank you.

CHAIR THOMADSEN: We are way ahead of schedule at the moment. And as always, because there are people who may be coming in to listen to certain topics who are expecting it to be at certain times we really can't just go ahead. So we are going to be on a break now until 3:30 when we will talk about radioactive seed localization.

(Whereupon, the above-entitled matter went off the record at 2:12 p.m. and resumed at 3:30 p.m.)

CHAIR THOMADSEN: We are ready to continue on the topic we were just discussing of medical events, that we need to renew the Subcommittee

that reviews the medical events this Committee each year because we have lost a couple of the members from that Subcommittee.

And so, the new Subcommittee will be Steve Mattmuller and Pat Zanzonico, John Suh, myself, Michael O'Hara, Ron Ennis. And I think that it is it.

Is there anybody who was on the Committee last time that I have forgotten?

MS. HOLIDAY: Dr. Palestro.

CHAIR THOMADSEN: Oh, Dr. Palestro. Thank you. Right. There we go. I think that is the Committee then.

MEMBER LANGHORST: I have been on it in the past, but I am good with not being on.

CHAIR THOMADSEN: How many do we have? That would be too many, I think.

MEMBER LANGHORST: Right.

MS. HOLIDAY: So, by practice, Subcommittees should have six members or less. This is not a Subcommittee that makes recommendations per se. The Subcommittee just presents information on medical events. I think it is fine if you have more than six members.

CHAIR THOMADSEN: I think you're on it. Congratulations.

(Laughter.)

Is there anybody who wants to speak up?

(Laughter.)

MS. HOLIDAY: I have Dr. Ennis, Dr. O'Hara, yourself, Dr. Palestro, Dr. Langhorst. Who was the sixth person?

CHAIR THOMADSEN: Dr. Suh.

MS. HOLIDAY: Dr. Suh. Okay. So, that is six people.

CHAIR THOMADSEN: And Dr. Zanzonico.

MS. HOLIDAY: Thank you.

CHAIR THOMADSEN: Yes. We will name the people who aren't on that Committee.

(Laughter.)

Well, I think we are ready to proceed with our schedule here. It is a pleasure to introduce Michael Sheetz from the University of Pittsburgh to talk about radiation safety and regulatory issues of radioactive seed localization of non-topical lesions.

MR. SHEETZ: Thank you. I would like to thank the members from the NRC and the ACMUI for giving me this opportunity to speak on radioactive

seed localization, or RSL.

I must admit that, when I first heard of RSL, I thought to myself, why would anyone want to implant a seed in a patient just to localize a lesion for surgical removal? And then, I learned of the benefits that this technique has with respect to patient care. And so, I have become a proponent or a supporter of this procedure, as evidenced by my presence here.

Next slide, please.

RSL was developed in the late 1990s, the first clinical trials occurring in 2001. I would say, up until the last several years, most institutions adopting this procedure have been large medical institutions with broad scope licenses.

We initiated our RSL program in 2011. We now have one of the most active programs I think in the country. We are implanting over 100 seeds or 100 procedures per month at six different locations.

We have also sponsored several RSL workshops or seminars, one-day seminars for institutions interested in starting a program. Mayo Clinic has been offering RSL workshops for several years, and most recently, both MD Anderson and

Memorial Sloan Kettering are offering RSL workshops. And so, it has gained more attention and interest.

From my employment with the workshops, conversations with colleagues, presentations I have done at professional meetings, the feedback I am getting is that, primarily from limited scope licensees, is that strict compliance with the NRC licensing guidance document makes it difficult to establish a program, and some have even given up.

And so, my purpose here today is to try to point where certain revisions and changes to the licensing guidance can make it more relevant to the procedure, make it less burdensome for institutions trying to initiate a program, and allow entries to access of this beneficial procedure to patients.

Next slide.

The medical background, advances in technology and screening mammography have led to increased detection of microscopic breast lesions. The traditional method of pinpointing these areas of concerns is where a localization breast biopsy procedure where a radiologist places a thin guide wire into the area of concern, using ultrasound or mammography. The surgeon, then, removes the tissue

around the guidewire and sends it to pathology for analysis.

Alternative technique, RSL, in this procedure a radiologist a radioactive seed in the area of concern, again under ultrasonic or mammographic guidance. The surgeon then uses a gamma probe to locate where the seed and the lesion is for extraction. There have been a number of studies and publications showing benefits of RSL over the wire localization procedure.

Next slide.

An example of the wire localization procedure with the image on the left, the radiologist places a needle to the center lesion and, then, inserts a guide wire with a barb on the tip to hold it in place. The wire extends outside the skin of the breast. The patient then goes to surgery, where the surgeon makes an incision at or near the protruding wire and uses it to guide the excision of the tissue. On the right is an image of the excised tissue with the wire still attached. These two procedures are performed on the same day.

Some of the disadvantage of wire localization is that it can pull out; it becomes

lodged and gets transected during surgery. The surgeon needs to use the wire as his or her point of entry in the surgical procedure. There is patient discomfort, and there are time delays in scheduling between the radiological procedure and the surgical procedure.

Next slide, please.

With RSL and iodine-125, seed is used which is the same type as that that is used for brachytherapy such as in prostate implants. The seed is now available in sterile, pre-loaded, 18-gauge needles. These packaged seed assemblies are available from two different vendors with full FDA approval for the localization procedure. So, it is no longer an off-label use of a brachytherapy source.

Initially, it was an off-label use, and institutions had to buy seasoned bulk and load their own. Now they have let the approval for this procedure, at least from two institutions.

The average activity that is used in the seed is around 200 microcuries, although that ranges from about 75 to 300 microcuries. At the bottom you can see what the assembled device looks like. There is an 18-gauge needle with a stainless steel sleeve

around for shielding the radiation from the seed. There is a blue spacer that holds the stylet that is inside the needle in place. And then, the seed is secured in the needle with bone wax, so it doesn't fall out the tip.

Next slide, please.

The seed is implanted at the center of the lesion by a radiologist under ultrasonic or mammographic guidance by advancing the needle to the center of the lesion. Then, the stylet is used to push the seed out and deploy it into the breast.

Once positioned, the seed cannot be repositioned, and then once it is in place, there is a very rare incidence of this seed migrating, even if it is left in for several days.

Next slide, please.

Immediately following that, a mammogram is taken to verify the implant location. We also perform a survey at this time, or actually before the mammogram, where we will take a GM Survey Meter and we will hold it up to the breast, so that we get a single and confirmed that the seed has been implanted. And then, we will also survey the implant tray and the implant area, so that we make sure we do not

detect any activity therein.

The patient is released with instructions to return for the scheduled surgery, usually within five days. We do not provide any radiation safety guidance to these patients, as it is not required; they are releasable and the exposure from these patients is very, very low.

Next slide, please.

On the day of surgery, the surgeon uses a gamma probe to localize the seed. This is the same instrument that the surgeon uses for sentinel lymph node biopsy with technetium-99m sulfur colloid.

The device is set on an I-125 window, so it can detect the photon energies of the I-125. The detector has a collimator on it, so it can look at it as a focused beam of radiation coming from the seed. And so, the surgeon can see in 3-dimension where the seed is located and where the lesion is located in the breast, and thereby choose the best approach in how they want to excise this tissue.

Most of these patients also have technetium sulfur colloid onboard for a sentinel node biopsy. Typically, the seed is removed first, and the sentinel node biopsy is performed after with the

axillary resection.

Next slide, please.

The gamma probe that is used provides audio feedback and it guides the excision during the whole process. Once the seed and tissue is removed, the surgeon will put the probe up to the tissue, make sure they get a strong signal indicating that the seed is present, and they will take the probe and put it into the cavity to confirm that they don't see any radioactivity and there is no activity left back into the patient.

Next slide, please.

At this point, a specimen radiograph is taken not only to confirm the presence of the seed, but also to confine the margins and confirm that all the suspicious tissue has been completely removed. The specimen is then transported to pathology for seed removal. However, some institutions at this point actually have the surgeon removing the seed from the specimen.

Next slide, please.

In pathology, the pathologist or pathology assistant will use the same gamma probe to scan the specimen and locate where the seed is

positioned within the specimen. They will then section the specimen into grade-thin 4-millimeter, 5-millimeter slices.

Next slide, please.

Once the seed is visualized in one of the sections, they will use reverse-action tweezers to remove it. The seed is, then, typically placed in some type of container labeled with an Rx or tracking number.

There is also, then, a survey performed of the remaining tissue specimen to make sure there is no activity in it. The seeds are, then, disposed of either through decay-in-storage or some institutions will actually disinfect the seed at this point and return it to the manufacturer.

Next slide, please.

Some studies show a reduced incidence in positive margins. With a positive margin, that means that there is still cancerous tissue close to the edge or at the edge of the tissue sample that was removed. It requires a repeat surgery. Repeat surgery positive margin incident rates vary greatly from surgeon to surgeon and institution to institution, but they are somewhere in the range of

5 to 20 percent. So, it is not insignificant as far as this repeat rate and requiring new surgery.

With RSL, the surgeon can approach the lesion from an angle. And so, this results in better cosmetic outcomes. There is less pain and discomfort for the patient, because once the seed is implanted, the patient doesn't feel anything.

And one of the largest advantages is that it decouples the radiology procedure from the surgical procedure. And so, delays in the breast center don't, then, cause delays piling up in the surgery center. Also, too, it allows for first-morning surgeries now; whereas, before that would not be possible.

Next slide, please.

RSL is covered under 35.1000 since it really doesn't fit in any of the other medical use categories. The NRC issued licensing guidance for RSL in 2006. To my knowledge, it has not been revised since then.

At that time, it was an off-use of the same seeds used for brachytherapy. So, it makes sense that the focus of the initial guidance would be to view this as a therapy procedure. However, even

though RSL uses the same seed as that used for brachytherapy, albeit at a lower activity, this is a localization procedure performed that is very similar to the technetium-99m sulfur colloid localization for sentinel lymph nodes under 35.200. It should be noted that RSL is the only non-therapeutic procedure addressed under 35.1000.

There are also certain regulatory requirements in Part 35 that will apply to RSL, such as patient release, leak tests, decay, and disposal of seeds, instrument calibration, and so forth. So, there are other regulations still in Part 35 that are applicable and don't need to be addressed in the licensing guidance.

Next slide, please.

I feel that the main issues to be addressed with respect to how RSL is performed and was being required in the licensing guidance are the training and experience requirements for the AU and individuals working the supervision of the AU; the need for a written directive; radiation surveys and their documentation; what would constitute a medical event for RSL; survey instruments used for this procedure and their calibration requirements, and

commitments to certain safety precautions in Part 35 that may not be directly applicable to radioactive seed localization.

Next slide, please.

In the guidance document, an individual qualifies to be an AU for RSL if they meet the requirements in 35.490 for manual brachytherapy or a radiation oncologist. However, this procedure is not performed by radiation oncologists, as they are neither trained nor credentialed to perform this procedure.

For a radiologist to be qualified as an Authorized User, they must meet the requirements in 35.290 for unsealed sources and be supervised in three cases by a 490-approved Authorized User. I would question whether it is appropriate for an individual to supervise casework for an implant procedure that they themselves do not perform.

There is a requirement for participation in three cases by the Authorized User. This can be difficult to obtain in institutions that are just starting out with the procedure where no one is an Authorized User. And so, then, who becomes the supervisor?

Also, it is not practical for the person attempting to be an Authorized User to go to another institution where RSL is licensed because most likely they will not have clinical privileges there to perform that procedure under an Authorized User at that other site.

Consideration should be given to accepting observance of cases to meet this three-case requirement or attendance to an RSL workshop to meet this requirement, or consideration should also be given to removing the three-case requirement to be an AU, as there is little or no precedent for it for any other localization procedure or any other non-therapeutic procedure.

The guidance document also requires the Authorized User to have experience in the surgical incision and seed removal. While the AU should be knowledgeable in the procedures that the surgeon is performing and the pathologist is performing, again, they cannot perform these procedures as they are neither trained in that nor credentialed to perform those. I know of one Agreement State where they were insisting for the AU to get this work experience and actually perform these procedures.

In the same sense, the surgeons that are working under the supervision of the Authorized User, in the guidance document it wants them to have training or preparation in implanting the seeds. Again, I will say surgeons are not qualified to prepare and implant seeds. And so, while they should be knowledgeable in the implant procedure, they themselves can't have actually hands-on work experience performing that.

Several statements in the guidance document imply that only an Authorized User implant seeds. As I have previously explained, the RSL procedure involves three different components. One, implanting a radioactive seed in a patient under mammographic or ultrasonic guidance by a radiologist. Two, surgical removal of a target lesion and seed from the patient by a surgeon. And three, removing the seed from the tissue specimen by a pathologist or pathology assistant.

Therefore, many, if not all, of these procedures with RSL are being performed by individuals working under the supervision of the AU. And so, this should include a radiologist who is not an AU, but has appropriate training experience to

implant seeds. Radiologists, by training, implant clips to mark biopsy sites. They implant wires for the localization procedure. And so, implanting a radioactive seed is an equivalent procedure for radiologists.

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The procedure does not meet the requirements for written directive as identified 35.40(a). The sources are not intended to deliver a therapeutic dose for palliative, curative treatments.

It would take nine days to deliver a dose of 50 rem at 1 centimeter from the seed with a 200-microcurie seed. While this is not a therapeutic dose, it is the dose threshold for a medical event.

Also, the documentation requirements for written directive in 35.40(b) sets demanded by the therapy simply are not applicable to the radioactive seed localization procedure. If a non-AU implants the seed, they would not be permitted to sign the written directive.

It may be appropriate to require a prescription to document the isotope ascribed implant site total number and activity of seeds implanted, time range of scheduled surgery date, and the name of

the approved radiologist who implanted the seed.

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Now I have previously explained surveys are performed after the seed implant with a GM Survey Meter, and in the surgery environment and in the pathology environment, surveys are performed with the gamma probe. Documentation is usually maintained as part of a checklist and not as a separate survey document.

Also, it should be noted that, if one tried to perform surveys on the OR, in pathology, with a GM or a thin crystal sodium iodide detector, that there will be interference from technetium if the sentinel node biopsy procedure was performed.

If a confirmatory radiograph was obtained following the implant, should this be allowed to substitute for radiation survey, as it will visualize and confirm the location of the seed and even if it was damaged? Similarly, a radiographic image taken of the specimen after it has been surgically removed from the patient could substitute for a radiation survey. So, there are different means and avenues to accomplish this.

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Consideration needs to be given as to what criteria would result in a medical event with RSL procedures. A dose threshold of 50 rem to tissue is unlikely. From the chart, you can see that the dose at 1 centimeter from a 200-microcurie seed would only be 28 rads if left in for five days.

Once you realize that when the seed and tissue is removed, there are several centimeters of tissue surrounding the seed that is excised, and so, the dose further out to the tissue that is remaining in the patient would be much less. In this case, at five days at 3 centimeters from the seed, the dose would be down to 2 rads.

There is no prescribed dose for radiation seed localization. There is an activity range of the seeds to be implanted.

As far as implant time, it is based on a recommendation that we want to perform the surgery within a certain amount of time. If the patient does not return for the surgery -- I know there was a discussion on this earlier, on what constitutes patient intervention -- but there are two different situations.

One which has occurred is the patient is

implanted with the seed and they come down with the flu, and so, they can't come back within five days because they don't want to do the surgery. So, the surgery is delayed for two or three weeks. I would contend that that would be patient intervention. It is out of anybody's control and they are going to recover the seed later.

If the patient refuses to come back to have the seed removed, then you may question, was there reasonable instruction to the patient to ensure that they would return? And so, I am not advocating any particular stance on what constitutes a medical event. I am just throwing out different situations that need to be thought-through and better defined on what constitutes a medical event for RSL.

And there was one case where the seed was intentionally left in the patient because of the location of the seed where it had migrated into a highly-vascularly area. And so, certainly, you would expect that to qualify as a medical event and being reported. So, I am not saying there are no medical event reporting criteria for RSL.

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There are three main radiation meters

used for RSL, the thin crystal sodium iodide and GM Survey Meters and the gamma probe. The guidance document recommends a survey instrument with a thin crystal sodium iodide; reverse-surveys are performed. While this is certainly the instrument of choice for trying to locate a lost seed, if you don't know where it is and no other activity is around, the GM Survey Meter works great on the implant side, again, checking that the seed has been implanted in the patient, checking the seed is in the needle. And the gamma probe works fantastic in the OR environment as far as locating the seed and, again, double-checking it is not in the patient. And again, it is the same with pathology. So, consideration should be given for the other instruments.

Most gamma probes do not require any routine annual calibration. They only have a system check when the instrument is turned on. So, they don't fit the normal calibration requirements in 35.60 and, in fact, the thin crystal sodium iodide detector does not fit the instrument calibration requirements in 35.60 as it typically reads out in counts per minute and not mR per hour.

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There is a section in the guidance document for a commitment to certain safety procedures for RSL. There is a commitment to verify the activity prior to seed implant using a calibrated instrument. There should be allowance now for allowing vendor verification of the seed activity.

There is a commitment requested to provide annual training on topics described in 35.410. This training is for personnel caring for patients who have been implanted with brachytherapy seeds and cannot be released into 35.75. These topics are not applicable to RSL, and these patients are released under 35.75.

If a licensee uses the radioactive seeds that are currently approved by FDA for this procedure, a custom evaluation of its use, off-label use, is not required.

Also, there is a lot of emphasis on routine monitoring before, during, and after all uses of the seeds to ensure rapid identification and remediation of a broken or a leaking seed, and emergency procedures and responding to sources that may rupture, retrieval of leaking/cut sources, contamination control, and decontamination of the

patient to carry out.

These seeds have been used for RSL procedures for over a decade and thousands of procedures, and without one case ever being reported of a cut or leaking seed implanted in patient. There have been seeds cut on the removal side, in pathology, but not on the implant side.

And so, while there needs to be appropriate instrumentation, procedures and response for cut or leaking sources, it should be realized that this is a very rare occurrence, and that the response by the same as that for contamination/decontamination in nuclear medicine.

Personnel are wearing personnel protective clothing on the implant and the surgical and the pathology side. So, there is personal protection. And any contamination of items would likely be contained with the bio-hazardous containment system.

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The guidance document may want to consider or have consideration for other procedures, have those events. One of these would be loss of the radioactive seed, implanting a radioactive seed in

the wrong patient or the wrong location, inability to locate an implanted seed during surgery, and there's been a planted seed in the patient but the patient does not return for the scheduled surgery. We have actually experienced three of the four.

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So, in conclusion, I believe that the RSL procedure provides significant clinical and patient care advantages over the standard wire localization technique. Strict compliance with NRC licensing guidance document makes it very difficult for limited scope licensees to implement this procedure. State regulators are not likely to vary from the stated guidance without specific approval from the NRC.

And I believe certain revisions to the guidance document can make it more relevant to the way the procedure is performed, make it less burdensome for institutions to establish an RSL program, and allow increased access to this beneficial procedure for patients, while maintaining a high level of safety.

Thank you.

CHAIR THOMADSEN: Thank you.

Comments from the Committee?

Dr. Costello? Mr. Costello?

MEMBER COSTELLO: Well, Sue promoted me to being a doctor earlier. So, I appreciate that.

What are the barriers to the radiologist being approved?

MR. SHEETZ: If they are boarded in radiology from 2007 forward, they would meet the requirements. But, if they are boarded prior to that, they would have to fill out the preceptor statement and document all of the training experience.

MEMBER COSTELLO: So, I was looking at your slide on Authorized Users. They wouldn't need to be supervised in three cases by a 35.490 Authorized User, right, because they would be an Authorized User if they were a radiologist?

MR. SHEETZ: No, if you are a radiologist and you have equivalent training for 35.200, you still need to be supervised in three cases by 490 or another Authorized User who is already approved for RSL. So, your 35.200 training experience criteria does not qualify you to be an Authorized User alone.

MEMBER COSTELLO: Because that is what the guidance says? Okay. This isn't 35.400 use; this is 35.1000 use. But they chose to use 35.490

as --

MR. SHEETZ: Correct, in this space, and understandably so, because at that time it was an off-label use of a brachytherapy source.

MEMBER COSTELLO: Okay.

MR. SHEETZ: I am not arguing that, but that is part of my reason for changing the focus.

MEMBER COSTELLO: Thank you.

CHAIR THOMADSEN: Other comments?

Dr. Suh?

MEMBER SUH: Do you have a rough sense of how many centers use this technique, this radioactive seed localization technique?

MR. SHEETZ: From conversations with one of the largest distributors, it is that they have 40 clients.

MEMBER SUH: Forty clients?

MR. SHEETZ: Yes, in the country.

MEMBER SUH: Do you have a broad sense of like how many cases per year in the U.S. that they do?

MR. SHEETZ: I do not have an idea of how many cases in the U.S. So, we are doing 1200, or whatever. Memorial Sloan Kettering is doing, in

fact, actually more than we are. They are doing a lot. I would say Mayo is probably close, third. So, it is times several thousands [of] cases per year.

MEMBER ZANZONICO: Right, and the only incident in thousands, one seed was cut in pathology?

MR. SHEETZ: I think the broad scope licensees have been doing this and they are the main user of this. But now, I think because of the articles that have come out, it is limited scope licensees that are trying to add this procedure, and this is where the difficulties come in.

It is really driven by the surgeons. The surgeons love this. It is not driven by the radiologists. It is driven by the surgeons.

CHAIR THOMADSEN: Ms. Weil?

MEMBER WEIL: Where do you get the data that this is a preferable procedure for patients from the point of view of discomfort?

MR. SHEETZ: Anecdotally, from patients that we have done both the wire and the seed. And so, this is the response back to the mammography/breast care imaging tech, that "Oh, wow, this seed was a piece of cake. This was great. I wish I had had this before as opposed to the wire."

MEMBER WEIL: And why do you have a mammogram immediately post-seed implant?

CHAIR THOMADSEN: It works with a wire with a hook on the end.

MR. SHEETZ: Sure.

MEMBER WEIL: But do you do the mammogram? Do you have to --

MR. SHEETZ: Uh-hum.

MEMBER WEIL: Yes?

MR. SHEETZ: Yes, there is still imaging with the wire.

MEMBER WEIL: Never mind.

(Laughter.)

CHAIR THOMADSEN: Okay. Dr. Ennis?

MEMBER ENNIS: Could you share more specifics about the purported advantages? There is, of course, no data, no real information about how much margins are better, how much pain is better, whatever the purported benefits.

MR. SHEETZ: I didn't really want to get into that. There are a number of studies. Some show advantages. Some show the procedures to be equivalent. But the numbers are small with all these studies. So, I don't think the verdict is out yet.

MEMBER ENNIS: Okay. So, at this point, is it fair to say the real advantage is the logistics for the surgeon?

MR. SHEETZ: Yes, that is the primary driver for it, yes.

CHAIR THOMADSEN: Dr. Dilsizian?

MEMBER DILSIZIAN: Great presentation. I just have many medical questions, just to help me to understand.

Usually, the biopsy, if it is malignant, then, you go in and put in the seed, correct?

MR. SHEETZ: Yes, they would do the imaging; they would see a suspicious tissue. They would do a needle biopsy.

MEMBER DILSIZIAN: First?

MR. SHEETZ: And then, they would drop a clip. Okay.

MEMBER DILSIZIAN: You mean you wouldn't wait until the official biopsy comes?

MR. SHEETZ: Yes.

MEMBER DILSIZIAN: For instance, first, you do the biopsy.

MR. SHEETZ: You do a needle biopsy.

MEMBER DILSIZIAN: If it is malignant,

then you go in and put in a beaker, right? I mean, you wouldn't just put it in if it is cystic abnormal?

MR. SHEETZ: Well, if there is suspicious tissue, they will do a needle biopsy, and then, they drop a clip, a marker clip, where they took the biopsy. And then, pathology does an analysis on the tissue, the needle biopsy.

MEMBER DILSIZIAN: Right.

MR. SHEETZ: And if that is cancerous or it is suspicious and they say, "We want to remove it," then, the patient comes back and either gets a wire or a seed for surgical removal of that tissue.

MEMBER DILSIZIAN: Okay. So, now it is malignancy and you are putting in a seed. My question is two-fold. One, you said that it would interfere with sentinel imaging, which if it is malignant, I mean, it seems to me that sentinel node would be an important quality assessment. Is that correct? Do you say that this would interfere or not with the sentinel technetium assessment?

MR. SHEETZ: No, this does not interfere with the sentinel node --

MEMBER DILSIZIAN: It doesn't?

MR. SHEETZ: Because the gamma probe has

windows for technetium and windows for the Iodine-125.

MEMBER DILSIZIAN: Sure.

MR. SHEETZ: Where I said it would be a problem or interference is if somebody used one of the other sodium iodide detector instruments to try to survey for I-125, and if there was technetium there for the sentinel node, they would get a signal from that.

MEMBER DILSIZIAN: I see. Okay. Thank you.

MR. SHEETZ: And so, they would not be able to serve the I-125.

CHAIR THOMADSEN: Mr. Costello?

MEMBER COSTELLO: You mentioned strict compliance; it is difficult, particularly to limited scope licensees. What particular changes in the guidance would you recommend?

MR. SHEETZ: Consideration of everything that I have stated here before you.

MEMBER COSTELLO: Well, for example, for an Authorized User how would we change that?

MR. SHEETZ: You could still have an Authorized User, either as a 490-approved radiation

oncologist or the 35.200, but not require the case requirements.

MEMBER COSTELLO: Okay.

MR. SHEETZ: They just have to be knowledgeable in the radioactive seed localization process from implant to surgical removal, to extraction, to inventories and surveys. Because they would be, then, the Authorized Users. Everybody else would, then, be performing the procedure, the radiologist, the breast care radiologist, and the surgeon and the pathologist, they would all be working under the supervision of the Authorized User.

DR. METTLER: At the end of the day, this is just the same as doing a sentinel lymph node. I mean, the surgeon has to chase it around. He has got to take it out. The pathologist has got to play with it.

MR. SHEETZ: Right.

DR. METTLER: And it is unsealed with the sentinel lymph node. This is sealed.

MR. SHEETZ: And most radiologists who perform the injection for sentinel lymph node are performing it under the supervision of your nuclear medicine physician. And we actually now have trained

our surgeons to perform the sentinel lymph node injections on the OR if the patient is put under anesthesia, to eliminate that pain. And so, the surgeons are actually performing sentinel lymph node injections under the supervision of the Nuclear Medicine Authorized User. So, this is no different. So, you have an Authorized user, but, then, a lot of the work is being performed by individuals under their supervision.

MEMBER COSTELLO: And I think you suggested that you don't need a written directive for this?

MR. SHEETZ: The written directive is not necessary.

MEMBER COSTELLO: But you also suggested that medical events are still possible?

MR. SHEETZ: That is correct. That is possible. Again, I am not advocating anything. I can see certain situations where a seed is left in.

MEMBER COSTELLO: And you ascribe it.

MR. SHEETZ: And ascribe it.

VICE CHAIR ALDERSON: So, I have a question which some of the people who use this procedure now widely can perhaps answer and, then, a

comment.

So, the question is, in institutions like your own, like Sloan Kettering, where this has begun to be used widely, it is judged by those physicians and the people involved that it is so much better? Has it replaced the wire? That is the first question. Has it replaced the wire?

MEMBER ZANZONICO: At Sloan Kettering, as far as I know, it has replaced it. It is the standard now. There are some instances where they still use the wire, but that is my understanding.

MR. SHEETZ: Yes, it has essentially replaced it.

VICE CHAIR ALDERSON: Okay.

MR. SHEETZ: Except for a very rare occurrence.

VICE CHAIR ALDERSON: All right. So, that's good. I mean, that suggests that a lot of knowledgeable people who use this think it is a good thing to do. I have no experience with this technique at all.

MEMBER ZANZONICO: There is a lot of enthusiasm, as you said, among the surgeons.

VICE CHAIR ALDERSON: Right. So, I am

going to mention a concern that will make you think I am extremely conservative, and this knowledgeable body can say, "Eh, forget about it now."

But I understand that the radiation range is small. The thing I am concerned about, or that my conservatism makes me be concerned about, is it is radiation. So, this is a relatively new procedure now. So, we haven't had much time. But, if in a few years some women come back and they have a new cancer and it is somewhere in the region of where they had the radioactive seed localization before, are some of our legal friends going to go after this, the same way they went after asbestos, and make it into something we turn around and say, "We wish we had never done that."?

Now that is, again, probably extraordinarily conservative, but we haven't had much time yet. So, anyway, I thought I should say it.

MR. SHEETZ: In response to that, I think if you look at the dose to the tissue that is remaining after the seed and the lesion have been excised, the radiation dose to that tissue is on the order of two view mammogram.

VICE CHAIR ALDERSON: Okay.

MR. SHEETZ: So, it is very low.

VICE CHAIR ALDERSON: So, it is just a couple hundred millirems, yes. All right. That is a good answer.

CHAIR THOMADSEN: Other comments?

Yes, Mr. Bollock.

MR. BOLLOCK: Thank you.

I would just like to add that the NRC and the Organization of Agreement States are forming a working group to update the guidance. Actually, Ms. Holiday is part of the working group, along with a representative from the States of New York and Utah. And we have one other NRC staff that hasn't been identified yet. But we are going to do that, hopefully, begin that in April.

CHAIR THOMADSEN: Begin that in April and finishing it when?

(Laughter.)

MR. BOLLOCK: If somebody can help me out with what's the estimate?

MS. HOLIDAY: Well, in all honesty, I can't really put a timeframe on it. It really does depend on deliberations and discussions of that working group. April is actually when we are hoping

to kick off the working group. We are still waiting to identify one additional member. And then, of course, you have to work around people's schedules. We are approaching summer vacation.

But I would just like to remind the Committee, with our most recent 35.1000 device, that is part of the toolkit, that only took us nine months to develop guidance. But that doesn't mean that we could be done in nine months. It could be earlier. It could be later. But I don't want to put a definitive number on that.

CHAIR THOMADSEN: My question has the intention of, when would you have to have this Committee's input in order to have it considered in the discussions?

MR. BOLLOCK: Yes, again, that would be dependent upon when the working group finishes their deliberations. So, I mean, it would be a guess, but it wouldn't be the next meeting. It would be after some few months at least, if they begin next month, that they would be ready to turn it over to ACMUI to review.

CHAIR THOMADSEN: Thank you.

Yes, Dr. Mettler?

DR. METTLER: So, can you tell me how this is any different from a sentinel lymph node other than it is a sealed source in terms of hazard or anything else?

MR. SHEETZ: And my viewpoint is it is no different.

MEMBER ZANZONICO: The one tact that strikes me is in the event -- and again, it would be patient intervention. A patient doesn't return. You are talking about considerably higher local radiation doses apropos the point that Dr. Alderson raised. I mean, the doses would be much less than a sentinel lymph node.

But those aren't trivial if they are local. It depends upon the volume for your calculation.

MR. SHEETZ: But these are the same seeds that are used for brachytherapy at three to five times greater activity where 50 to 100 are implanted in the prostate, and it is not infrequent for one to migrate to the lungs or the bladder or become dislodged somewhere else in the body and remain there until they decay away.

DR. METTLER: Plus, the people pee them

out.

MR. SHEETZ: So, a single left in the body is not going to cause any extra --

MEMBER ZANZONICO: No, I don't disagree. I am just playing devil's advocate.

MR. SHEETZ: Yes.

MEMBER ENNIS: Well, it would depend on where it was. I mean, if it was right under the skin, it actually would, a superficial region.

MR. SHEETZ: Okay.

MEMBER ENNIS: And if the patient didn't return, they would have an ulcer and it would be a problem.

CHAIR THOMADSEN: Ms. Weil?

MEMBER WEIL: I just have to put this out there. From listening to this, it sounds like the primary driver for this particular therapy is that it is extremely convenient for the surgical schedule because it doesn't have to be done in tandem with the radiologist doing a localization with a wire. There isn't that proximity in time that has to be factored into it.

If that is the primary reason for the popularity of this particular procedure, it would be

nice to have more data about its satisfaction levels for patients as opposed to satisfaction for the clinicians involved.

CHAIR THOMADSEN: Dr. Langhorst?

MEMBER LANGHORST: But this discussion is really a request to update NRC's licensing guidance for this. It is not to make any changes and, hey, everybody needs to have this. It is to update a 2006 guidance document, with the many years -- I mean, this has been used for 10 years now -- with the current way of doing it. And so, that is what is being brought to our --

MEMBER WEIL: Yes, this presentation, though, is about how wonderful this is, not about -- I mean, it is about both things. It is about a recommendation for changing guidance or a request for that, but it is also about how terrific this particular procedure is.

CHAIR THOMADSEN: Yes?

MR. SHEETZ: I agree with you; one of the main benefits is the decoupling of the scheduling conflicts.

The second is that the surgeons can see where the seed is. And so, they can choose where to

make the incision to remove the lesion, as opposed to having to follow the wire in. So, there is definitely cosmetic outcomes by using the seed because they don't have to follow the wire. They can come where it is not going to be as revealing.

And so, even the surgeons that were not onboard with this early on, once they started, they said, "Okay, this was great because I can get better cosmetic outcomes." So, I think that is the second big driver for this.

And the positive margins and reduced volume of tissue, and all that, it is probably equivalent.

VICE CHAIR ALDERSON: I have a follow-up question.

CHAIR THOMADSEN: Yes, go ahead.

VICE CHAIR ALDERSON: And I was reading your slides to see if it was here and I just missed it. So, say it again. What are the specific changes that you seek in the guidance? It just says here you want the guidance to be changed. What are the specific changes that you seek?

MR. SHEETZ: The primary one would be the training and experience requirements for the

Authorized User. Maybe discontinuing three cases or allow them to observe cases or allow them to attend a workshop and they would automatically qualify as an Authorized User, whether they are 35.200- or 35.400-approved.

Recognition that radiologists with training in the procedure can implant the seeds under the supervision of an Authorized User because the guidance document right now implies that only an Authorized User implant seeds. And some institutions are following that. They looked at that and said -- and some regulators are requiring that. So, they won't allow a radiologist to implant the seed under the supervision of an Authorized User. That means everybody has to become an Authorized User.

VICE CHAIR ALDERSON: So, those are those are the only two things you see?

MR. SHEETZ: No. The other was the elimination of a written directive requirement.

VICE CHAIR ALDERSON: Yes, no written directive.

MR. SHEETZ: And the other was my third-to-the-last slide on the commitments that are required in the guidance documents for other

regulations in 35 that really are inapplicable; you know, 35.410, and things of that nature.

VICE CHAIR ALDERSON: I see. And do you believe, in addition to a radiologist being able to implant under the direction of an AU, what about surgeons? Can they do it under an AU?

MR. SHEETZ: Do the surgical procedure?

VICE CHAIR ALDERSON: Do the implantation?

MR. SHEETZ: No, they don't have the training to implant seeds nor would they be medically credentialed. A surgeon can't implant a seed in a hospital.

MEMBER WEIL: They remove them.

MR. SHEETZ: They remove them.

DR. METTLER: But, in one sentence, if you had that one sentence, it would be: treat this procedure just like you treat a sentinel node procedure; everything the same?

MR. SHEETZ: Yes.

DR. METTLER: Excepting if they don't come back to get this thing taken out, though. Other than that, everything is the same. In fact, let's say it is at least sealed as opposed to unsealed.

MR. SHEETZ: Well, it would fit perfectly under 35.200 except it is sealed.

MEMBER COSTELLO: The one medical event -- I'm sorry -- that you described where basically you couldn't remove the seed because of where it was located, if I recall, right?

MR. SHEETZ: I'm sorry? What?

MEMBER COSTELLO: The one medical event that you referred to --

MR. SHEETZ: Yes, yes, right.

MEMBER COSTELLO: -- if that had happened with technetium, would that have been a medical event?

MR. SHEETZ: I'm not sure what you mean by technetium. The sentinel node injection stays there or --

MEMBER DILSIZIAN: No, the exposure.

MEMBER COSTELLO: Okay.

MR. SHEETZ: The exposure?

MEMBER COSTELLO: As far as the exposure. So, the exposure in a case with these was hot, turned out to be hot, or would have been --

MR. SHEETZ: If left in indefinitely or for a certain period of time, correct.

MEMBER COSTELLO: Right.

MR. SHEETZ: This is a long half-life.

MEMBER COSTELLO: So, the doses can be higher here if they stay there longer, assuming they can't get them out?

MR. SHEETZ: Correct. As I said, it would be nine days for 50 rads at 170.

MEMBER COSTELLO: Right.

DR. METTLER: But, at the end of the day, if you infiltrate an FDG dose, you know, you have got local doses of the same amount.

MEMBER COSTELLO: Thinking infiltration, Think as an acceptor for infiltration, right?

DR. METTLER: Yes, I mean in terms of biological events.

MEMBER COSTELLO: Sure.

MR. SHEETZ: And I am not arguing that if the seed is left in or a patient doesn't return, that that shouldn't be reported as a medical event.

MEMBER COSTELLO: What I struggle with is, conceptually, possibly having a medical event without the written directive, because the two are linked together.

CHAIR THOMADSEN: Mr. Mattmuller?

MEMBER MATTMULLER: Well, I would say

that is not possible because, for example, we had where the patient was accidentally injected with a full multi-dose vial of, I think it was technetium NBP, and there was no written directive for that diagnostic procedure. But, yet, still a medical event occurred.

MEMBER COSTELLO: Thank you.

CHAIR THOMADSEN: Now any other comments?

MS. THOMAS: Are you asking for comments on the bridge line?

CHAIR THOMADSEN: Yes, on the issue of breast localization with radioactive sources.

Okay. I would like to name a Subcommittee to develop recommendations on the issues raised by this presentation. So, it would be making recommendations on radioactive seed localization to present to this Committee. The timeline would be before the next Committee meeting. We may have to have a conference call, depending on how quickly the working group is getting together and discussing this. Whether or not the presentation would be before the next Committee meeting is irrelevant. The work needs to be done quickly.

And I would like to ask Dr. Ennis to be

the Chair of that Committee. I would like Dr. Alderson to also be on that Committee and Mr. Costello to be on that Committee.

Do we have volunteers who would like to be on that Committee as well?

Dr. Zanzonico. I would like to name Dr. Mettler as soon as he gets his final approval and clearances, and whatever.

It should happen before the Committee makes its report.

Any other comments on that?

MEMBER COSTELLO: Could you go through those names again, please?

CHAIR THOMADSEN: Dr. Ennis, Dr. Alderson, Mr. Costello, Dr. Zanzonico, and Dr. Mettler conditionally. I think that is what I said.

Okay. No other comments on this topic?

Yes?

MEMBER LANGHORST: I just want to make mention as to how Mr. Sheetz came to give us this talk. He reached out to the NRC to ask about the licensing guidance. NRC's staff was fabulous in trying to direct him to the right place. I know we talked with Mr. Costello and, eventually, it came to

me. My name is on there just because I tried to help facilitate this.

But I really want to encourage the people who listen to our Committee meetings, who read our transcripts, and so on, that you have available to you an opportunity to suggest topics and even come talk to us.

I really appreciate Mr. Sheetz's efforts in educating me on this process because we do not do it at Washington University at this point in time. And I really appreciate him coming out to talk to us about this.

CHAIR THOMADSEN: Dr. Mettler?

DR. METTLER: A great presentation.

MR. SHEETZ: Thank you.

DR. METTLER: You must have a library of references that might be in PDF format about all of this? If you could get it forward --

MR. SHEETZ: I certainly can.

CHAIR THOMADSEN: Thank you. Thank you very much.

MR. SHEETZ: Thank you very much. I appreciate it.

MS. HOLIDAY: Dr. Thomadsen?

CHAIR THOMADSEN: Yes?

MS. HOLIDAY: Is this okay? I just wanted to make one comment. I just wanted to say this is a prime example of -- I know we have said it before -- but for all items that are licensed under 35.1000, there is that caveat where all these guidance documents are located that there is an opportunity for the general public, staff, anyone, if you feel that there should be changes, that you can contact us to let us know. Because these are essentially living, breathing documents.

As we all know, microspheres guidance document has undergone several revisions, as I am sure we will go under another revision with this most recent Subcommittee report that we received at the last meeting.

So, as Mr. Sheetz indicated, this guidance document was created in 2006. As time goes on, we learn more about what these modalities can do. If there is stuff that we had in there before that is no longer applicable or if there is stuff that should be in there, help us help the medical community. That is what we rely on you for; that is what we rely on the medical community to tell us. We can't do our

jobs if you don't tell us.

Thank you.

CHAIR THOMADSEN: Thank you. Point well taken. Thank you very much.

And now, to round out the day, we have Mr. Mattmuller to tell us about germanium/gallium generators and their decommissioning.

MEMBER MATTMULLER: Good afternoon, everyone.

I am Steve Mattmuller, and I will be presenting our Subcommittee report. But, first, I just wanted to make a couple of general comments on comments I have already heard today that I really appreciated.

Laura's initial comments reminding us of our responsibility to help advise/guide the NRC for appropriate regulations, so they are perfect for medical care and patient care and don't interfere with patient care.

Also, I really appreciated the comment Dr. Mettler made, and then confirmed by Dr. Thomadsen, that we are to be pests to the NRC, if need be the case.

(Laughter.)

DR. METTLER: Advice.

MEMBER MATTMULLER: Advice? It sounded like "pests" over here on this side of the room.

DR. METTLER: It reminds me of my children. What I said wasn't necessarily what I meant, and what you heard wasn't what I said.

(Laughter.)

MEMBER MATTMULLER: Okay. So, first of all, I would like to review why germanium and gallium-68 are so important to the field of nuclear medicine, the charges to the Subcommittee, and its responses to the charges.

Next slide, please.

So, here's a comparison, images of a PET drug versus a spec drug. You can see the dramatic advantages the PET drug offers of the gallium-68 DOTA on the right versus the older spec agent, indium-111 DTPA octreotide on the left.

Greater image quality, greater diagnostic sensitivity and accuracy. There is actually faster imaging time. The gallium-68 image can be acquired in one day for the patient versus the two days it takes for the indium study. And there is also a lower radiation dose.

Another exciting developing for the gallium-68 right in pharmaceuticals is the relative ease of how you can substitute, you can bring in a therapeutic radionuclide such as lutetium-177 into the very same molecule. So, then, you actually transform a very sensitive, specific diagnostic drug into a very sensitive, specific therapeutic drug. And they call this aspect theragnostics, the combinations of a diagnostic/therapeutic drug.

For this type of drug, for the DOTAs, in particular, they call this peptide receptor radionuclide therapy, or PRRT.

Next slide, please.

So, here is a list of most, not all, of the different areas where gallium-68 is now being used or under investigation. So, you might ask, how big is this iceberg really, especially in today's years or time zones and climate change? But it is big.

As an example, last weekend was the Third World Congress of Theragnostics Gallium-68 and PRRT held last weekend in Baltimore. This is the first time it has met here in the U.S., as especially in Europe, gallium-68 use is mainstream; whereas, in the

U.S. it is still investigational.

The boat is at the tip of the iceberg. It is used to image somatostatin receptors found in neuroendocrine tumors, or NETs, N-E-T. And as stated by Dr. Zanzonico in a past meeting, the DOTAs are really just the tip of the iceberg. Also, in the U.S. they are the closest to be acquiring FDA approval.

In the middle of the iceberg -- I hope you can see it -- is prostate imaging using an agent PSMA. That is also getting a lot of attention worldwide. Again, great images and a much larger patient population. It would be my prediction as the next drug after the DOTAs to receive FDA approval.

And at the base, which is maybe a little bit hard to read -- I'm sorry -- are the theragnostics. Again, the development of therapeutic drugs from the diagnostic drug.

Next, please.

This is our source of the gallium-68, the generator. The parent radionuclide is germanium-68, a solid on a dry column about the size of my little finger. The germanium-68 decays to the daughter radionuclide gallium-68. To remove it, one elutes

the column by passing dilute hydrochloric acid through the column and it is a collection vial. But germanium-68 is left behind on the column; the gallium-68 collects in the vial.

Now, even though she is a pre-K teacher, my daughter assured me that no one could go wrong with show and tell.

(Laughter.)

So, this is an actual prototype of the Eckart & Ziegler generator. This is what we are talking about. It is very small. It requires no power, no electrical cord, no batteries. There are no moving parts. It is rather kind of boring. It just sits in a lead-shielded area.

This helps explain why the previous image of the iceberg is so big. PET radionuclides have terrific imaging advantages over spec radionuclides. But most of the PET radionuclides need a cyclotron just to produce them, and cyclotrons are big and expensive. Actually, you would need a room about the size of this meeting room for a cyclotron, its support areas, and chemistry areas, and quality control areas.

You might think of this little generator

as a mini-cyclotron in a box, but it has regulatory issues -- and that is why we are really here -- as the germanium-68, the parent radionuclide, triggers a decommissioning funding plan.

Next slide, please.

And here it is for a decommissioning fund plan in part 35.35. "Each applicant for a specific license authorizing the possession and use of unsealed byproduct material" -- and, currently, the germanium is considered unsealed -- "with a half-life greater than 120 days" -- it does have a half-life of 271 days -- "and in quantities exceeding 10 to the fifth times the applicable quantity set forth in Appendix B," it meets these three conditions and you need to get a DFP for your gallium generator or for any radionuclide.

Briefly, a DFP describes what happens to the facility after it closes, after you lose or terminate your possess license. Equipment, structures, and portions of the facility containing radioactive contaminants will be removed or decontaminated to a level that permits release of the property. Basically, it has to be cleaned-up to the original background levels.

So, a DFP is very extensive and expensive to create, to get approved, and also to fund. And it is a continuous burden, as it needs to be reviewed, resubmitted, and reapproved every three years for as long as the license is active. It is a big burden. It requires a lot of man-hours and a lot in terms of financial assurance.

Next slide, please.

This really is a curious regulatory situation for us, as we have two identically labeled appendices in 10 CFR, quantities of licensed material requiring labeling, but they contain two different lists. Appendix C in Part 20 has over 600 radionuclides, and B in Part 30 has less than 200. Appendix C, you might guess, is the newer version of the two.

And for the first two radionuclides that we are all familiar with, F-18 and molybdenum-99, the two appendices have the same values. But the problem is our germanium-68. There is a boundary of 10 microcuries in Appendix C, but there is no value listed for germanium in B. And this is the missing piece of our regulatory puzzle.

So, from the previous regulation, it says

you take this number, list it in B, multiply it by 10 to the fifth power, and that is your limit for activity to determine whether or not you have to get a DFP.

But, without a value in the appendix, you have to use the default-level value of 0.1 microcuries, which, when you do the math, gives you a limit of only 10 millicuries. That is a problem because these are typically 50-millicurie-sized generators.

It gets more curious. The last time Appendix B was amended was 1980. But check out these two redesignations, which means it gets moved, not amended, but just to a different part in the regulations.

From 1991 to 1993, this was a transition period for the implementation of the then-newly-revised Part 20. So, we have the new Appendix C and the new version of Part 20, and Appendix B from Part 30 gets moved over to Part 20 as the old version. So, during these two years, there are two versions of Appendix C, an old and a new, and there is no version of B in Part 30. That amended Part 30 to say, if you need to calculate a DFP, then look for your value in

the old Appendix C in Part 20.

In 1993, the transition period is over. So, it is just a new version of Part 20 is valid, and the old version of C is moved back to Part 30 and becomes Appendix B again. So, here to the old and, then, back.

Unfortunately, with all this, which is not clear why that happened, there still isn't a value for germanium-68. So, it is puzzling because we are not sure why. At one point, they had a reference in Part 30 to say, if you need this value, go to Appendix C. Why they didn't keep that I don't know. Or why, then, they moved the old Appendix C from 20 back to become Appendix B again of Part 30, why that appendix wasn't revised and amended to include a value for germanium-68?

So, another part of the puzzle is in 2005, when the definition of byproduct material is expanded to include accelerator-produced radionuclides such as the PET radionuclides F-18 and germanium-68. This is the original occurrence when there were a couple of licensees that had gallium generators in 2004, and in 2005 they were told, "You now have to have a DFP."

But, overall, trying to figure this out,

this rabbit hole of regulations, I am still not 100-percent sure what really happened to our core value. As best as I can say, it was an unintentional omission for B or, as you might say, it got lost in translation.

Next slide, please.

So, the charges given to the Committees were to evaluate the cost of a DFP, to provide examples of regulatory relief, and to evaluate how a DFP might affect future clinical use of gallium-68.

Next slide, please.

So, the first attempt was to try to figure out what does a DFP cost. Several large commercial nuclear pharmacy firms were contacted, and we also found a couple of health physics consultants on the internet who advertised their DFP experience and expertise. We contacted them also, asked for an estimate on what it would cost to prepare or fund a DFP for a medical license, not a firm number, just an estimate. We heard nothing from nobody.

So, I thought, all right, I will just try to do it myself. You know, a do-it-yourself attitude. How hard could it be, right?

(Laughter.)

And this slide is actually a little bit inaccurate because it just lists one volume of NUREG-1757. After I prepared this slide, I actually found two more volumes of this guide and, ironically, is titled "Consolidated". And the three guides total 1,349 pages of guidance.

So, the DFP covers, as I have said before, not just the use of germanium-68, but all uses of radioactive material at all locations under the license. So, a hospital, if they have a cyclotron, PET chemistry areas, PET spec imaging areas, a hot lab with a technetium generator, satellite imaging sites within the building, outside of the department, or satellite imaging areas outside at different locations in the town, local area, or even in another hospital with its own nuclear medicine department, if those are all under the same license, as is the case at my hospital, they all have to be considered in the formation/calculation of the DFP.

Or, for a commercial nuclear pharmacy, a number of them have cyclotrons and PET chemistry areas. That would dramatically increase their cost for a DFP.

In fact, that did happen in 2004. There

was a commercial pharmacy that had a cyclotron and had a gallium-68 generator for research. When they were told to get a DFP, they looked into it, but it is going to cost them $15 to $20 thousand a year every year. So, they got rid of the generator.

So, our charge is about a question asked. It is really a very expensive question to answer. And it is also very unreasonable to expect anyone to do this on a voluntary basis. So, in hindsight, I am now not at all surprised that I didn't hear from any of those other firms. So, this may be pictured as an RSO as he tries to push a round through a square hole.

Next slide, please.

We do, however, have a very detailed narrative from an RSO as he tried to prepare a DFP for a large, multi-site university-based hospital. In the next couple of slides, the quotations marks all are comments from this RSO.

Next. Yes.

"Resource demands go far beyond the cost associated with the generation and maintenance of a financial assurance instrument itself, which can be in the thousands of dollars in creation fees and more thousands in annual maintenance fees. It is a very

expensive effort to prepare it."

He had to review the regulations and guidance, all 1,349 pages. He had to review research, the historical use for all buildings and locations, obtain cost estimates for the various actions required that required any decommissioning process, calculate person-hour involvement for all man-hour costs related to these actions, and determine and estimate waste disposal cost, time demands for the creation of the worksheets and spreadsheets, writing and compiling a plan for related internal and external communications.

Next, please.

His initial estimate, substantial cost in manpower from the Operations and Safety Office. He calculated 140 hours. So, it sounds maybe somewhat manageable.

But, then, he soon adds -- next, please -- "I'm probably underestimating this. He sums up his experience as "extensive and expensive".

Next slide, please.

There are also significant manpower costs to the institution for other areas involved, such as risk management, insurance, finance, facilities,

administration, and legal.

Next, please.

Once submitted, the DFP has to go to the State, in his case, to be approved. And he states, "This puts significant resource demands on regulatory agencies related to review an ultimate approval of the DFP." So, I think that is a pretty insightful observation on his part. A DFP also puts a big demand on states, who already have very limited resources in dealing with radioactive material licensees.

Next, please.

For example, the State's initial review resulted in comments that required yet additional demands that he estimated cost them an additional 30 person-hours.

And that, ultimately, for his institution, financial assurances owed of $1.125 million.

In addition, this burden still doesn't end because, if they go this route, they still have to revise, resubmit, and get it reapproved every three years.

So, what happened at this institution? Ultimately, they decided the DFP was going to cost

too much. So, they didn't do it. So, they had to scale-back their research plans to use a used generator smaller than 10 millicuries in size, so they wouldn't have the DFP.

But all their research is limited to just imaging in smaller animals, mice, rats, versus what they had initially planned to do was image in patients, research subjects.

So, trying to push a round ball through a square hole does have consequences. That's clear.

Many hospitals will not have the in-house expertise to deal with the DFP issue. And if they do have to pursue DF Planning, they will likely need to hire consultants, adding further to their costs, one more additional potential barrier in cost. A RSO really understands what it takes to prepare a DFP for a medical institution.

The restrictive aspects arising from the current Part 30 situation may, therefore, prevent or deter use of promising imaging agents for patients due to the decommissioning funding burden. This concern is exactly our concern.

Next, please.

So, the little RSO has given up on the

ball, and now he is thinking about our second charge, regulatory relief.

The simplest and best way would be to add the same value of 10 microcuries for germanium-68 that exist in Appendix C, Part 20, to Appendix B, Part 30. A simple solution, as both appendices have the same title, "Quantities of Radioactive Material that Require Labeling," but how?

Perhaps the best would be using a Direct Final Rulemaking or DFR, and these can be used for noncontroversial rulemaking, as this issue would certainly be. Its advantage is that it takes much less time than a typical rulemaking of 10 to 12 years.

However, from the DFR guidance, it typically deals with safety or security concerns. So, this really isn't a safety concern or a security concern. This is a patient concern.

Since the unintentional omission of a value in Appendix B for germanium, a DFP is now required for the possession of a generator. And the cost of a DFP can be a prohibitive financial barrier to the license and will deter the safe and effective use of gallium in patients.

The next slide, please.

On the upside, fortunately, DFR guidance is much shorter than DFP guidance, but there are five questions we have to answer.

The first question is, what has happened, what has changed that causes the current regulation or policy to be insufficient? Appendix B has actually been unchanged since 1980. What has changed is the recent dramatic increase in the use of gallium-68. Remember the iceberg.

Next, please.

Suzanne said this succinctly: increase in the use of gallium-68.

Next, please.

What information causes the NRC to question the current regulation or policy? We are now very aware of the man-hour and financial burden of a DFP and how this has already deterred the use of gallium in research and more than likely will deter the use of gallium-68 in clinical patients.

A nuclear pharmacy and a contract research organization stopped their research after 2005. And more recently, a large university hospital curtailed their research use.

Next, please.

So, to answer this, a DFP's deleterious effects.

Next, please.

The third question is, what is the regulatory insufficiency or gap that needs to be addressed?

Next, please.

The missing value in Appendix B.

In '93, why in 30.35 wasn't the reference to Appendix C, Part 20, kept, as it would have referenced the new version of the appendix? Or why wasn't Appendix B, Part 30, amended to be consistent with the new C -- they had the same title -- with the value for germanium-68?

Next, please.

So, the fourth question is, why does the insufficiency or gap warrant being addressed? The FDA and the NRC are both responsible for the regulation of radiopharmaceuticals, but this responsibility has to be balanced, in that on one side of this responsibility is to ensure the safe and effective use, but the other side's responsibility is to avoid creating artificial barriers and unnecessary barriers to the use of these drugs.

Next, please.

Patient access. The last question, please. Why is a change needed if there is no gap to be addressed?

Next, please.

The gap does exist and it has very expensive consequences.

Next slide, please.

So, still thinking about alternates and guidance, and I really think a DFR would be the best route, but if the NRC wants a choice, what if the NRC were to reconsider this generator as a sealed source within a device? As such, we could avoid the DFP requirements.

So, if you looked at the current sealed source device guidance -- next, please -- which is NUREG-1556, it could fit as a custom sealed source or device. As a custom, what is attractive here in the guidance, if it stays under 200 millicuries, which it could, and if the reviewer decides applicant has training and experience to handle the material in unsealed -- that is not a typo -- unsealed form, one would not have to rely on the intrinsic safety of the sealed source to demonstrate compliance. It just

sits there. That is all it does.

Next, please.

Or it could fit under a sealed source and device for medical uses. Now, currently, in guidance for medical use, it says the device has to have one of four types of FDA approval, and it won't have any of these four types.

But this is NRC guidance, not FDA guidance. So, it could be revised to include the generator as a medical source device.

If the guidance is revised, it is now a sealed source device where it could fit in the regulations. It could fit under 32.74, and I expressly want to read in Section (a)(2)(iii) where "results of the prototype testing demonstrate that the source of the device will maintain its integrity under stresses likely" -- and that is underlined; emphasis has been added -- "to be encountered in normal use." So, unlike a sealed seed that is implanted into a patient, a much more stressful environment than what this will ever encounter. This sits in a box.

Or, it could also fit under 35.1000, "Other Medical Uses of Byproduct Material or

Radiation from Byproduct Material". It is definitely another.

Next slide, please.

So, let's address our last charge, effect on clinical care because of a regulatory quirk, an unintentional omission.

Next, please.

We know of a DFP's negative effect on three licensees already in regards to research, the most recent, a large, university-based hospital. And we really can't say it any better than the RSO.

Next, please.

To paraphrase him: may prevent or deter use due to the DFP's funding burden.

And as a reminder, we are getting closer to clinical use here in the U.S. The DOTAs, which are used in NET patients, one of the DOTAs is already in active discussions with the FDA to determine the best pathway forward for approval, and you might remember, as an orphan drug, this is not uncommon for the FDA to assist sponsors for these orphan drugs.

So, it is really not a question of if there will be an approved gallium-68 drug, but really a question of when. The zebra ribbon, the NET patient

groups use it for public awareness and as a metaphor for the difficulty they experience in getting their disease diagnosed. If you hear hoof beats, it may not be a horse, but a zebra.

Next, please.

NET cancers are very difficult to diagnose. After the onset of symptoms, which are often non-specific and vague, a diagnosis can take an average of three to seven years. It would be tragic for patients in the U.S. who are suffering from neuroendrocrine disease to be given one more burden in coping with their disease.

So, while this issue may not be safety-significant in a traditional NRC way, i.e., a risk of people or to the environment, I can guarantee you it is very significant to the patients who suffer with neuroendocrine disease.

Next, please.

I have added this web address to remind us why we are here, as sometimes it is lost to get in the regulations we come across. I urge you to check this out at a later time.

It is from a NET patient support group, and there are pictures of patients holding out

placards with a number on it, and the number represents how long it took them to get a correct diagnosis. It is really pretty sobering, especially in this day and age of modern medicine.

The NRC does have a responsibility, and that is not to be burden to these or to any other patients.

One more time, please. Thank you.

So, three cold facts to remember about our iceberg: the drugs will be the first of the gallium-68 drugs here in the U.S. to be approved. Worldwide interest is a big driving force. There will be more gallium-68 drugs approved in the future, and it is time for the NRC to act now and not later.

And at the base, again, the large potential for theragnostic or therapeutic drugs is also driving interesting in gallium-68.

Next slide, please.

So, to summarize, to evaluate the cost of a DFP, it is prohibitive. It is very expensive just to create a DFP. They are specific to license. No two will be alike.

Next, please.

Relief.

Next, please.

A DFR, a Direct Final Ruling, or revised guidance.

Next, please.

Will the future clinical use of new radiopharmaceuticals be affected? Yes, it will, of course.

First, the neuroendocrine tumor patients will be affected, and then, more than likely, the prostate cancer patients.

And really, I should put our little RSO figure at the top, as his narrative and his experience was invaluable for preparing this report, especially his final words of "may prevent or deter use due to the DFP funding burden".

We believe the NRC needs to act so as to avoid the consequences of an unintentional omission in the regulations from becoming an unintentional burden on patient care. To eliminate this burden, we would recommend that the NRC should notify the licensees as soon as possible, stating that "Regulatory relief from a DFP requirement for a gallium-68 generator is now in progress. It will no longer be required. Effective immediately, no

licensee will be required to submit a DFP for a gallium-68 generator."

Thank you.

CHAIR THOMADSEN: Thank you very much, Mr. Mattmuller.

Comments from the Committee?

Yes?

MEMBER ZANZONICO: I just have a question. You had mentioned that a DFP is not isotope-specific. In other words, you have a DFP covering all the isotopes in an institution?

MEMBER MATTMULLER: Right. In everybody's situation right now, the DFP is triggered by the possession of the gallium generator. But, once you need a DFP, it, then, covers all radionuclides, all locations under that license.

MEMBER ZANZONICO: So, that is why it escalates the cost?

MEMBER MATTMULLER: Right, right, right. It would be a much different situation if it was just the box that is sits in.

MEMBER ZANZONICO: And one other question. There is no other regulatory vehicle, like a surety bond or such a thing as that in place of an

actual DFP? Or are they the same thing?

MEMBER MATTMULLER: The surety bond is the financial assurance portion --

MEMBER ZANZONICO: Okay.

MEMBER MATTMULLER: -- of the DFP.

MEMBER ZANZONICO: So, that would be a component of the DFP?

MEMBER MATTMULLER: It is a component of it, right.

MEMBER ZANZONICO: That is all part of it?

MEMBER MATTMULLER: Right.

CHAIR THOMADSEN: Mr. Costello?

MEMBER COSTELLO: There are a number of elements. There is the cost estimate in which the RSO had talked about he looked at all the labs that had isotopes of a half-life longer than 120 days and you get their area and look at their history, and so forth. And you develop a cost estimate.

Then, you have the Decommissioning Funding Plan, which is how you are going to fund the cost estimate. And then, you have the instruments. So, you are talking about a surety bond or whatever it is. These are all the instruments to fund the

Decommissioning Funding Plan.

CHAIR THOMADSEN: Thank you very much.

Dr. Mettler?

DR. METTLER: You keep saying this was an unintentional omission.

MEMBER MATTMULLER: I believe so.

DR. METTLER: How do you know that? You know, there are people who have been in the NRC forever, I hear.

(Laughter.)

I mean, somebody did this. And so, there must be some memory out there.

MEMBER COSTELLO: Remember that the purpose of this table, this table has been back in Part 20 since the dawn of time, I mean, probably back to the fifties, okay? It is a safety purpose. Okay? It is telling you what qualities of radioactive material are required to be labeled.

The purpose where these tables were shaded, there was no requirement for financial assurance. Okay? It was just to cite what has to put a label on that bottle, or whatever. Basically, that was considered to be a small quantity, a not-very-hazardous quantity.

And so, if financial assurance came along, they didn't want to be reinventing the wheel and come up with their own table. So, they said, "Oh, we'll use that table as a multiplier of that table." I think the lowest multiplier is 1,000 times, which you get your certain amount of financial assurance, and you have to have 10,000 times and 100,000 times, okay?

The purpose of the table, nothing to do with financial assurance. My question from the very beginning when we talked about this is, you have the table in Part 20 and the table in Part 30 both saying, you know, what the requirements are. Why have two tables?

The original purpose of those tables is not financial assurance. It is telling universities or whatever when they have to label things. By and large, they are all the same.

Of course, back in 1980, or whenever, there was no energy jurisdiction. If there had been, we wouldn't be having this problem, but there wasn't.

DR. METTLER: But, still, everybody is sure that it was unintentionally --

MEMBER COSTELLO: Sure, I think you have

a little bit of insight about there were some discussions, maybe not?

MEMBER LANGHORST: As an RSO that went through the new Part 20 implementation in the early 1990s -- I believe I was nine years old then -- it was understood, I mean, I don't even remember the part about Part 30 and that table changing.

But, in going back and re-reading that Federal Register, I understood why the NRC wanted to use the old values while implementation was happening with the new Part 20 because licensees had the option to implement it at any given point in time, I think, within a two-year period.

But, at the end of that two years, you assumed that that Part 30 table would, then, switch to reference the new Part 20 Appendix C. But, instead, it got put back into Part 30 and, unfortunately, in that Federal Register the Part 30 table was not reprinted. It just referenced it, and then, it appeared in the next year's Code of Federal Regulations. So, that table wasn't reprinted as the old table in Part 30 in that Federal Register of the change of the final Part 20.

This also confusing, and I have been

confused by it as we have been reviewing it, because I thought a mistake was made, but then, no, it wasn't a mistake. But it certainly is goofy.

DR. METTLER: Okay. Well, in any case, I haven't heard for sure that it was unintended. I haven't heard the proof that it was unintentional.

But, be that as it may, the next question I would have is, if one isotope got lost, are there other isotopes that have gotten lost? I'm sure there are. I mean, how many isotopes are there in the Part 20 version?

MEMBER MATTMULLER: It is 600.

MEMBER COSTELLO: And how many in the Part 30 version?

MEMBER MATTMULLER: Less than 200.

(Laughter.)

I mean, but the question would be, of those 400, which have applications to nuclear medicine for either diagnosis -- well, if they are going to have a half-life greater than 270 days, they were thinking therapy or such.

MEMBER COSTELLO: A hundred and twenty days is like financial assurance. But maybe there are isotopes in there that aren't being used now that

sometime in the future could be. I don't know.

DR. METTLER: Well, yes. I mean, it seems to me, if you are missing one that became useful, there might be other ones that are missing that could become useful. If you are going to fix this, why fix it for just one as opposed the other potential issues?

MEMBER COSTELLO: I totally agree.

CHAIR THOMADSEN: Dr. Langhorst?

MEMBER LANGHORST: Fixing it would mean rulemaking, and our children here around the table could be discussing this. I think the relief right now that is needed is for one identified isotope and the encouragement to get this fixed on a wider basis for future isotopes used in medicine would be helpful.

DR. METTLER: Okay, but it seems to me, rather than calling this sealed source or whatever, the simplest thing to do is say you need a number that is going to get you to 50 in this table, period.

MEMBER COSTELLO: And take the number from the other table, and they're good.

MEMBER MATTMULLER: If you take the number from the newer version, from Appendix C, that will give us a limit of 100 millicuries, which is

twice the value of a 50-millicurie generator.

DR. METTLER: And what would it take to put the number from that table into this table? Or, I mean, that doesn't need a rule. That just needs somebody in the Commission to go do it.

(Laughter.)

DR. HOWE: It requires rulemaking.

MEMBER MATTMULLER: To address your other concerns --

CHAIR THOMADSEN: Yes?

MEMBER MATTMULLER: -- I also serve on the Isotope Committee for the Society of Nuclear Medicine and Molecular Imaging. To be honest, most of the time we do talk about this little radionuclide called molybdenum-99.

But this is where this issue came up a couple of years ago with germanium. To my knowledge, this is the only one on our radar screen, so to speak, that has an almost-immediate medical/clinical use that is going to be held back because of the DFP.

MEMBER COSTELLO: As some people have seen my emails on this, okay, I say it is not the ''what'' or the "why" that we are talking about; it is the "how". I mean the "why" is very clear and the

"what" is very clear. The question is, what regulatory mechanism gets us from here to there the fastest?

It is really an NRC question. You know, it is their rulemaking process. It is their everything process. But it should be whatever is fastest to make that number say 100 should be taken.

DR. WAHL: Hi. This is Dr. Wahl. I am calling in. May I comment?

CHAIR THOMADSEN: Yes, please.

DR. WAHL: Yes. I'm Richard Wahl. I'm Director of the Mallinckrodt Institute of Radiology in St. Louis. I am a nuclear medicine physician and radiologist.

I have looked at the discussion. I just wanted to reiterate what Mr. Mattmuller has said. I was a Co-Chair of the Third World Gallium Congress this past Thursday, Friday, and Saturday in Baltimore. We had over 200 scientific registrants and an additional 70 patient participants with neuroendocrine tumors.

From that meeting, it is abundantly clear that the gallium-68 radioisotope will play an important and growing role in patients with

neuroendocrine tumors and likely prostate cancer, as he pointed out.

And the neuroendocrine tumors are an orphan indication. And the patent position on some of the agents is not so clear. But it is quite clear that it is a very limited market. The FDA has recognized this and provided some regulatory relief specific to orphan drugs.

Clearly, the requirement for DFP for a drug that is not used in very many patients is a huge burden on academic medical centers or whoever has to install the generators, perhaps commercial pharmacies.

But these stands clearly are better than what we have available now. And interestingly, the radiation death to patients from these particular types of standards are substantially lower than from the currently-available tests. The results are more accurate and the patients have the results more quickly and they are likely cheaper.

There are many good things and many reasons to have this technology available. Certainly, I don't think the NRC would want us not to have the methodologies available. And this relief in

some way from the DFP for the germanium generators appears logical and appropriate using methods that you can best figure out, but it needs to be done expeditiously.

I had such a system up and using it in patients at Johns Hopkins, where I worked until a few months ago. I have recently moved to St. Louis, and we would like to get this going here. We are working on it, but the cost of a DFP will be a barrier to our implementing this, even at a large academic center.

So, I just wanted to reiterate how medically important this is and how there are so many barriers already; we really don't need one more to prevent patients from receiving this isotope.

Thank you.

CHAIR THOMADSEN: Thank you very much.

We also have another caller who wanted to make a comment.

Josh Mailman, are you on the line?

MR. MAILMAN: Yes, I am on the line. I am Josh Mailman. I am the Chair of Patient Advocacy for the Society of Nuclear Medicine, and I also run 501(c)(3) nonprofit for neuroendocrine support in Northern California.

And I wanted to echo Dr. Wahl's comments as well and also say that, while the incidence is rare, the prevalence is actually much more widespread than we think of. We have 150,000 patients in the United States that are living with neuroendocrine tumors.

With the very short half-life of gallium-68, it will mean that the gallium-68 will need to be produced near where the patients are as opposed to having it shipped in, like we are currently doing with indium-111. So, it will be of great patient benefit to have it near where the patients live and not just at certain compounding pharmacies or pharmacies that can send things out to different centers. So, it is challenging if it is just going to be at a couple of very large centers around the United States and not have access at the regional locations as well.

CHAIR THOMADSEN: Thank you very much.

I think we have a comment here.

MS. BUNNING: Okay, thank you.

I am Sue Bunning. I am with the Society of Nuclear Medicine and Molecular Imaging.

I think everything pretty much has been

said. I want to thank the Committee that has looked at this. This is a very important issue to the Society.

I think, Steve, you mentioned the Committee within SNMMI that has been working on this. He's right, this is the only isotope that has been brought to our attention. We are hearing a lot on this issue.

The Theragnostic Congress last week, I also had the pleasure of attending it. And Dr. Wahl is right, there were about 300 folks there. In addition to the patients asking often, "Okay, what's happening at the FDA to get this through," we receive a lot of questions about why do we still have to keep going to Europe.

And the patients often encounter problems with their travel. I think Josh on the phone could fill you in on some of those.

But they want to see this widely used in the United States. Right now, I believe there are approximately 10 or 11 centers that are under IND. But our hope is that this gets widely distributed throughout the United States and the patients will have access to this.

So, thank you. We support the work that you are doing, and thank you very much for letting me speak.

CHAIR THOMADSEN: Thank you.

I think the case has made that we should try to do something about this. And I will put it to the NRC: what would be the most efficacious way to address the issue?

MR. BOLLOCK: Yes, that is a tough one to answer, which would be the fastest. I mean, there are options. There are multiple options. Petitions for rulemaking. There are requests for relief from the DFP and giving the reasons why. And, yes, us going through and changing our guidance documents. I don't know which one has the shortest timeline. A lot depends on what is the process and how much we have backing any opposition, especially for the rulemaking, any opposition.

CHAIR THOMADSEN: Mr. Mattmuller, you had a comment?

MEMBER MATTMULLER: Right. So, I would like to ask, is it possible that why don't we let staff figure out what is the preferred route they would like to go to get relief? Can the Commissioners

put out a notice saying that relief is coming and, effective immediately, you no longer have to pay attention to DFP requirements, as in the future it won't be required?

MR. BOLLOCK: We do have a few options. I know I can think of one option.

Sophie, do you want to chime-in?

MS. HOLIDAY: I just want to say, as the Subcommittee knows, I was the appointed NRC contact person for this Subcommittee. And so, while the Subcommittee was doing their research, and Dr. Langhorst made the trail on all the old Federal Register notices, I did speak to some of our counterparts here.

Originally, it was believed that there was an omission. Some staff had believed that was the case; other staff did not.

So, I think it would be inappropriate to expect for the Commission to issue something to say, "We will grant relief immediately." Because, just like anything, you have to do your research very thoroughly before you go out and do anything like that.

It is also like when NRC publishes

Regulatory Issue Summaries or Information Notices, you can't just do it on a whim. You have to make sure you are putting out the correct information.

So, Sophie's suggest would be for the Committee to put forth a recommendation. And that way, we can say the ACMUI has made this recommendation. And that would give us the language that we need to go forth and say, "Hey, given what our priorities are, how can we fit this in? Because we have heard from the ACMUI. We have heard from members of the public. We have heard from professional organizations regarding this generator. What do we do now?" So, that would be my suggestion.

MEMBER COSTELLO: Can the NRC recommend to the Committee what we can recommend to you for the "how"? Because we don't know the "how" as well as you folks do.

MR. BOLLOCK: Right, and, I mean, the "how" would be -- you could recommend to us to find out what our options are, and then --

MEMBER COSTELLO: We can do that now.

(Laughter.)

MR. BOLLOCK: That's right. Like I said, I mean, there are options.

MEMBER COSTELLO: I don't know a "how," but --

CHAIR THOMADSEN: Dr. Langhorst?

MEMBER LANGHORST: A question I have on the request for relief, is that a licensee-by-licensee request or --

MR. BOLLOCK: I believe so. I believe it is licensee-to-licensee, unless we did come up -- I know Sophie mentioned the RIS, Regulatory Information Summary -- unless we saw a number of those or a group got together and put it in. That may be a pathway that we would like to take.

MEMBER COSTELLO: And the solution has to work in the Agreement State, which is where the licensees are.

MR. BOLLOCK: Uh-hum.

MS. HOLIDAY: I would also like to point out that at the last meeting Ms. Dudes, she did a lot of contribution for the discussions that took place. And she said, in order for us to move forward with any type of action, we need to know how many potential licensees does this affect. And without us knowing, to say, "Oh, there are three institutions that this impacts," NRC wouldn't necessarily, to be efficient,

we wouldn't just say, "Here's a blanket exemption." But, if it is only three, then those three individual institutions may get relief on an individual basis. It is kind of like when we do exemptions. It is on a case-by-case basis.

But, if we do truly believe that it is affecting a wide range of licensees, we have to be able to make that justification. Similar to how we do our rulemakings, a regulatory basis has to be formed.

CHAIR THOMADSEN: Right, although we do have the problem that, if you are looking at how many licensees this may affect, you are not getting any data on those people who would be licensees but are being deterred by the current regulations.

MS. HOLIDAY: Right.

MEMBER MATTMULLER: Right. It is sort of like a-chicken-or-an-egg question. But the three I mentioned were involved in research. And so, technically, we don't have an approved drug yet. So, we don't know about the official effect on clinical use.

And I attended the meeting last weekend, too. If you see the interest that these new drugs

generate, you know it is going to happen. So, when it does happen, I would hate to see this requirement slow it down.

CHAIR THOMADSEN: Dr. O'Hara?

MEMBER O'HARA: So, the drug isn't cleared, isn't approved by CDER yet?

MEMBER MATTMULLER: Not yet, no.

MEMBER O'HARA: Is there an indication where it is in the review?

MEMBER MATTMULLER: I don't know the exact answer to that question.

MEMBER O'HARA: Yes. I was just wondering.

MEMBER MATTMULLER: Yes.

MEMBER O'HARA: Because once CDER would approve it, approve the drug, my estimation would be there would be a lot more demand.

MEMBER MATTMULLER: Right. Of course. In the DOTAs' advantage, in their corner, I mean, they have extensive data. They have been used for over a decade in Europe. So, there is a lot of safety and efficacy data already generated for the drug. So, it is not like they are reinventing the wheel for the data to support the application.

CHAIR THOMADSEN: The big rush will come when CMS approves it.

Yes, Dr. Langhorst?

MEMBER LANGHORST: So, you don't have any -- do you think in a year? It could happen next month? You really don't know?

MEMBER MATTMULLER: That's a question I would to love ask the FDA representative to answer.

MEMBER O'HARA: And I can't answer it.

MEMBER MATTMULLER: So, no, no.

MEMBER O'HARA: I can't answer it now.

MEMBER LANGHORST: Right. And even if he could, he couldn't.

(Laughter.)

MEMBER MATTMULLER: Well, that is a whole other issue, yes.

MEMBER LANGHORST: A recommendation that I might suggest is that we have an ACMUI teleconference soon, like in the next two months, that NRC staff can come back and provide us with what are the "how's" that we can follow.

CHAIR THOMADSEN: I think that is a good idea, but I will amend that to suggest that the Committee go back to work, and maybe based on European

experience, try to come up with an estimated number of potential licensees that there may be who would want to do this.

And with the support staff member -- do you have a support staff member yet?

MEMBER MATTMULLER: Yes, Sophie.

MEMBER LANGHORST: Sophie is that support staff.

MEMBER MATTMULLER: Of course.

CHAIR THOMADSEN: With the help of your support staff person, consider the possible remedial actions that could be taken to provide relief, to make a recommendation to this Committee. So that, when we do have our call, we have something to work with, rather than just start talking.

Ms. Weil?

MEMBER WEIL: Would it also make sense to have statements from the related professional societies supporting the changes that we are suggesting, to add those to our recommendation?

CHAIR THOMADSEN: Oh, I will ask Mr. Bollock. Should they bother with that now?

MR. BOLLOCK: Well, I think the more people you have behind it, it gives more weight to

the broad scope. And so, three licensees -- if there is more interest --

CHAIR THOMADSEN: Dr. Mettler?

DR. METTLER: Me knowing nothing about the process, so if three groups ask for exemption -- is that what you are calling it? -- and they got it -- well, first, I don't know how difficult it is to apply for an exemption and get it. But, if you did that and got it, regardless of all this other process of trying to figure out what is going to happen in the future, the door would be cracked open already. And it would seem to me that would make the rest of the process go a lot quicker later.

So, do you see what I'm saying? I mean, I just don't know how difficult it is to get the exemption. But, once one person has the exemption or two --

CHAIR THOMADSEN: Ms. Cockerham, do you have a comment on that?

MS. COCKERHAM: Yes, just a general comment. Just from being around for a little while, I don't see OGC in the audience here, but they will not regulate by exemption. That is not a model that we use.

And so, the idea that the door would be cracked open and, then, the others could follow, it would be case-by-case and it wouldn't necessarily be based on precedent. And they are very, very hesitant to let us -- like I said, that is wide open, like we will not regulate by exemption. They will prefer that we go rulemaking or --

CHAIR THOMADSEN: Mr. Costello?

MEMBER COSTELLO: I believe that one of the institutions that thought about using it is in Pennsylvania. And they did, in fact, ask us for an exemption, and we said no, not me personally, but -- (laughter) -- me, institutionally, said no.

If the NRC grants an exemption to one of its licensees, I think that would make the Agreement States much more comfortable in granting exemptions. But, if the NRC has never granted an exemption, it would be highly unlikely that we are going to be on the cutting edge of exemption-granting.

(Laughter.)

CHAIR THOMADSEN: Thank you for that comment.

Do we have any other comments?

(No response.)

In that case, maybe what we also might do is, at our closing when we find dates for our next meeting, we also find a date for the conference call covering this, while we are all here. I think that will make Sophie's life a little easier.

Yes?

MS. THOMAS: I'm on the phone line.

CHAIR THOMADSEN: Yes?

MS. THOMAS: Are you open for public comment?

CHAIR THOMADSEN: On this topic?

MS. THOMAS: This is Ruth Thomas.

CHAIR THOMADSEN: Yes?

MS. THOMAS: And I have been listening with interest. I would like to ask for -- I am afraid it has to be hard copy because I don't have a computer -- but I would like to have either a transcript or the information that has been presented today, so that this can be made available to members of the public.

CHAIR THOMADSEN: I think that that can be arranged. Usually, the transcripts are reviewed and approved within, I think, 90 days of the meeting.

Is there a way for her to leave a

telephone number or an address with somebody?

MS. THOMAS: Well, this last part seems like it was going into a new area, and the gentleman that presented that, is he going to be making that available?

CHAIR THOMADSEN: I'm sorry, what did you just ask? Is he going to be what? Oh, are your slides available?

MS. THOMAS: The gentleman that came on -- I didn't catch his name -- and presented this different idea.

CHAIR THOMADSEN: Uh-hum. Could we get the hard copy of the slides along with the transcript sent?

MS. HOLIDAY: Yes. Ms. Thomas, I know that you have my contact information. So, please feel free to call me.

But, for everyone that is listening in, all of the handouts, which includes the meeting slides for all of the presenters, the meeting transcript, and the meeting summary are posted onto the ACMUI meetings web page, which you can access through nrc.gov. And if you do a search for "ACMUI" or even if you go to Google and you just type in "ACMUI

meeting," the link will pop up very quickly.

MS. THOMAS: Well, thank you very much. I appreciate that.

MS. HOLIDAY: You're welcome.

CHAIR THOMADSEN: Certainly.

MR. MAILMAN: Just so you know, this is Josh Mailman again.

Your actual web page went dead about 10 minutes ago, in case anyone is there. Actually, I see that it is connection lost.

Thank you.

CHAIR THOMADSEN: Thank you. But you have been able to be on the telephone line, it sounds like? Is that true?

MR. MAILMAN: Yes, the telephone line stayed alive. So, I have been on both.

CHAIR THOMADSEN: Okay. Thank you for that information.

Any other comments? Hearing none -- yes?

MR. BOLLOCK: I just want to add -- and this is on a personal safety basis -- with the forecast for tomorrow, the potential snow in the morning, so there is a potential for a mix of snow and rain; there is the possibility that the government

will have a two-hour delay. But we will still be able to start on time at 8:30 tomorrow morning.

And just a note for all of you here who have traveled, be careful, be safe out there.

CHAIR THOMADSEN: Thank you for that warning.

(Laughter.)

Any other announcements?

Yes?

MEMBER COSTELLO: Move to adjourn.

CHAIR THOMADSEN: What's that?

MEMBER COSTELLO: Move to adjourn.

CHAIR THOMADSEN: We're going to, then, adjourn until 8:30 tomorrow morning, where we plan on meeting promptly.

(Whereupon, at 5:28 p.m., the meeting adjourned, to reconvene the following day, Friday, March 20, 2015, at 8:30 a.m.)

STATEMENT OF PETER CRANE TO THE ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

MEETING OF MARCH 19, 2015, NRC HEADQUARTERS, ROCKVILLE, MARYLAND

March 18, 2015

To the Committee:

I appreciate the opportunity to submit this statement to the Committee, as it prepares for its meetings on March 19 and 20, 2015. I look forward to hearing the staff's report on the progress of the continuing studies, under contract to NRC, on radiation doses attributable to patients released under 10 CFR 35.75, the Patient Release Rule.

Through the RADSAFE online bulletin board, I recently learned that Dr. Carol S. Marcus, a former member of this Committee, filed a petition for rulemaking with the NRC on February 9, 2015.[1] I urge the members of the Committee and other concerned persons in the NRC community to give this document close attention. Not only is it of interest in and of itself, its extremism serves to illuminate the intellectual underpinnings of the Patient Release Rule, which derives from an earlier petition for rulemaking from Dr. Marcus, filed in 1990 and later amended. Regrettably, the Commission did not then appreciate the extent to which Dr. Marcus's views deviated from the mainstream.

Dr. Marcus begins by attacking the Linear No-Dose Threshold Theory (LNT). So far so good, one might say; the LNT is admittedly a theory which remains to be proven. Dr. Marcus goes beyond that, however, to disparage the expertise of bodies that advocate the LNT (she mentions "NCRP, ICRP, IAEA, and NAS-NRC's BEIR Committee"[2]) and the integrity of the "army of regulators at NRC, EPA, FDA, as well as DOE [who] would be unbudgeted if the LNT disappeared." She reveals herself as a passionate advocate of the "hormesis" theory, and cites with approval the claims of Professor Edward Calabrese that the LNT was based on "amazing misconduct by the nation's leading geneticists in mid-twentieth century."[3] She informs us that "the attitude of today's regulators is reminiscent of the Catholic Church at the time of Galileo. ... [T[he Church threatened to torture Galileo to death unless he rescinded his point of view. ... [W]hile today's regulators do not have the tools of torture available that the Catholic Church used, today's regulators will certainly destroy careers for regulatory violations of questionable importance."

I will leave it to those currently employed by NRC to decide whether they deserve comparison

[1] It can be found online at:
http://radiationeffects.org/wp-content/uploads/2015/03/Hormesis-Petition-to-NRC-02-09-15.pdf

[2] "NRC" in this context stands for the National Research Council.

[3] Anyone with an interest in unusual conspiracy theories can read Dr. Calabrese's views in an interview in which he asserts that the LNT was a deliberate lie, launched in the 1946 Nobel Prize acceptance speech of Dr. Hermann Muller.
http://www.21stcenturysciencetech.com/Articles_2011/Fall-2011/Interview_Calabrese.pdf

to torturers. I certainly didn't feel that way in my 23 years at the agency.

Next, Dr. Marcus reviews the scientific data: the Hiroshima and Nagasaki survivors, nuclear power plant workers, tuberculosis patients given fluoroscopes, radium watch dial painters, hyperthyroidism patients treated with I-131, persons exposed to radiation from the explosion of a nuclear fuel reprocessing plant in Russia in 1957, persons exposed to radiation from accidentally recycled cobalt-60 sources in Taiwan, and Americans exposed to low levels of radon in their homes. Again and again she finds a hormetic effect.

This reader of the petition immediately wondered, how will she deal with Chernobyl, which has caused over 7000 cases of thyroid cancer to date? The answer: it didn't happen. She writes:

> The affected population in the former Soviet Union was followed for increased cancer incidence. According to UNSCEAR 2000b [citation omitted] and the United Nations Chernobyl Forum in 2006, except for thyroid cancers in the highly contaminated areas, there was no increased incidence of leukemias or solid tumors, and no evidence of increased genetic diseases. The increase in thyroid cancers was found in children under the age of 15 years in 1987, the year after the accident. However, the radiation doses were too low to have caused this, and there was no dose-response relationship. In addition, the timing was off – the mean latent period for radiation induced thyroid cancer is about 28 years [citing the UNSCEAR 2000b report.] However, the increase was highly likely due to a mass screening effect [citation omitted]. Occult thyroid cancer is actually extremely common.... [petition at p. 6.]

The mainstream view of the Chernobyl data, of course, is that the appearance of so many thyroid cancers so soon after the accident (the first cluster of cases showed up near Minsk, Belarus, in about 1991, as I recall) was an indication that I-131 was more carcinogenic, when inhaled or ingested by the young, than previously suspected. Previously, the latency period was believed to be much longer. Dr. Marcus turns this on its head, however, arguing that since the latency period is much longer (a mean of 28 years, she says), the cancers found in 2000 and 2006 had to have some cause other than radiation, and can be attributed to better screening. Does that argument hold up? I will focus on just one part of the question: latency periods. Let us look, for example, at "Latency Period of Thyroid Neoplasia After Radiation Exposure," an article published in the journal Annals of Surgery in 2004.[4] It found, based on a relatively small sample, that the mean latency period for papillary thyroid cancer associated with external radiation was approximately 30 years, whereas the mean latency period for

[4] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1356259/
Ann Surg. 2004 Apr; 239(4): 536–543.
Latency Period of Thyroid Neoplasia After Radiation Exposure
Shoichi Kikuchi, MD, PhD, Nancy D. Perrier, MD, Philip Ituarte, PhD, MPH, Allan E. Siperstein, MD, Quan-Yang Duh, MD, and Orlo H. Clark, MD

post-Chernobyl cancer, associated with internal radiation, was about six years.

This is not the place for a detailed discussion of the Chernobyl data – I only learned of Dr. Marcus's petition yesterday, and the Committee's meeting is tomorrow – but there is ample scientific evidence that the post-Chernobyl thyroid cancers were caused by internal radiation exposure, and that there is a linear dose-response relationship. See, e.g., Risk of thyroid cancer after exposure to 131I in childhood, Cardis E et al., J. Natl Cancer Inst., 2005 May 18:97(10);: 724-32.[5]

Finally, we come to Dr. Marcus's proposed solution. Rather than characterize it, I will reproduce it in full:

> 1) Worker doses should remain at present levels, with allowance of up to 100 mSv (10 rem) effective dose per year if the doses are chronic.
> 2) ALARA should be removed entirely from the regulations, as it makes no sense to decrease radiation doses that are not only harmless but may be hormetic.
> 3) Public doses should be raised to worker doses, as these low doses may be hormetic. Why deprive the public of the benefits of low dose radiation?
> 4) End differential doses to pregnant women, embryos and fetuses, and children under 18 years of age.

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[5] Abstract

BACKGROUND:

After the Chernobyl nuclear power plant accident in April 1986, a large increase in the incidence of childhood thyroid cancer was reported in contaminated areas. Most of the radiation exposure to the thyroid was from iodine isotopes, especially 131I. We carried out a population-based case-control study of thyroid cancer in Belarus and the Russian Federation to evaluate the risk of thyroid cancer after exposure to radioactive iodine in childhood and to investigate environmental and host factors that may modify this risk.

METHODS:

We studied 276 case patients with thyroid cancer through 1998 and 1300 matched control subjects, all aged younger than 15 years at the time of the accident. Individual doses were estimated for each subject based on their whereabouts and dietary habits at the time of the accident and in following days, weeks, and years; their likely stable iodine status at the time of the accident was also evaluated. Data were analyzed by conditional logistic regression using several different models. All statistical tests were two-sided.

RESULTS:

A strong dose-response relationship was observed between radiation dose to the thyroid received in childhood and thyroid cancer risk (P<.001). For a dose of 1 Gy, the estimated odds ratio of thyroid cancer varied from 5.5 (95% confidence interval [CI] = 3.1 to 9.5) to 8.4 (95% CI = 4.1 to 17.3), depending on the risk model. A linear dose-response relationship was observed up to 1.5-2 Gy. The risk of radiation-related thyroid cancer was three times higher in iodine-deficient areas (relative risk [RR]= 3.2, 95% CI = 1.9 to 5.5) than elsewhere. Administration of potassium iodide as a dietary supplement reduced this risk of radiation-related thyroid cancer by a factor of 3 (RR = 0.34, 95% CI = 0.1 to 0.9, for consumption of potassium iodide versus no consumption).

CONCLUSION:

Exposure to (131)I in childhood is associated with an increased risk of thyroid cancer. Both iodine deficiency and iodine supplementation appear to modify this risk. These results have important public health implications: stable iodine supplementation in iodine-deficient populations may substantially reduce the risk of thyroid cancer related to radioactive iodines in case of exposure to radioactive iodines in childhood that may occur after radiation accidents or during medical diagnostic and therapeutic procedures.

It is safe to say that if the United States of America were to change its radiation protection regulations to allow children, fetuses, and pregnant woman to receive as much radiation as a worker in a nuclear facility, on grounds that we do not want to deprive them of the hormetic benefits of radiation, this country and the NRC in particular would, in the world radiation community, be laughingstocks.

Thank you.

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1356259/