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UNITED STATES OF AMERICA

NUCLEAR REGULATORY COMMISSION

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ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

(ACMUI)

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MEETING

+ + + + +

WEDNESDAY,

APRIL 20, 2005

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ROCKVILLE, MARYLAND

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The committee met at the Bethesda North Marriott Hotel and Conference Center, 5701 Marinelli Road, at 8:00 a.m., Leon S. Malmud, Chairman, presiding.

COMMITTEE MEMBERS:

LEON S. MALMUD, M.D., Chairman

DAVID A. DIAMOND, M.D., Member

DOUGLAS F. EGGLI, M.D., Member

RALPH P. LIETO, Member

SUBIR NAG, M.D., Member

ALBERT E. RAIZNER, M.D., Member

SALLY WAGNER SCHWARZ, R.Ph., Member

COMMITTEE MEMBERS: (cont'd)

ORHAN SULEIMAN, Ph.D., Member

WILLIAM VAN DECKER, M.D., Member

RICHARD J. VETTER, Ph.D., Member

JEFFREY F. WILLIAMSON, Ph.D., Member

NRC STAFF PRESENT:

THOMAS H. ESSIG, Designated Federal Official

ROGER W. BROSEUS, Ph.D.

IVELISSE CABRERA

DONNA-BETH HOWE

ANGELA McINTOSH

CHARLES L. MILLER

SAMI SHERBINI, Ph.D.

RONALD ZELAC, Ph.D.

ALSO PRESENT:

LYNNE A. FAIROBENT, AAPM

I-N-D-E-X

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

(8:13 a.m.)

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

My name is Thomas Essig. I'm Branch Chief of the Material Safety Inspection Branch and have been designated as the federal official for this Advisory Committee in accordance with 10 CFR Part 7.11.

Present today as alternate Designated Official is Cynthia Flannery.

This is an announced meeting of the committee. It is being held in accordance with the rules and regulations of the Federal Advisory Committee Act and the Nuclear Regulatory Commission. The meeting was announced in the February 28, 2005, edition of the Federal Register.

The function of the committee is to advise staff on issues and 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 them very much.

I request that whenever possible we try to reach consensus on the various issues that we will discuss today and tomorrow, but I also value minority or dissenting opinions. If you have any such opinions, please allow them to be read in the record.

As part of the preparation for this meeting, I have reviewed the agenda for members and employment interests based on the very general nature of the discussion that we're going to have today and tomorrow. I have not identified any items that would pose a conflict. Therefore, I see no need for an individual member to -- of the committee to recuse themselves from the committee's decision-making activities.

However, if during the course of our business you determine that you have some conflict, please state it for the record and recuse yourself from that particular aspect of the discussion.

At this point, I would like to introduce the members who are here today. Dr. Douglas Eggli, Nuclear Medicine Physician; Dr. David Diamond, Radiation Oncologist; Dr. Subir Nag, Radiation Oncologist. Would you raise your hand, Dr. Nag?

(Laughter.)

Dr. William Van Deck, Nuclear

Cardiologist; Ms. Sally Schwarz, Nuclear Pharmacist; Dr. Richard Vetter, Radiation Safety Officer; Dr. Jeffrey Williamson, Therapy Physicist; Dr. Albert Raizner, who is with us for the first time today, who is an Interventional Cardiologist; and Mr. Ralph Lieto, Nuclear Medicine Physicist; and Dr. Orhan Suleiman from the Center for Devices and Radiological Health from the Food and Drug Administration.

MEMBER SULEIMAN: Actually, that's Center for Drug Evaluation and Research.

MR. ESSIG: I still didn't get this right.

(Laughter.)

Okay. We'll fix it for next time. I updated some old notes.

Mr. Ed Bailey, who is our State Representative, and Dr. Robert Schenter, Patient Advocate Representative, were unable to attend today's meeting.

In accordance with the bylaws of the committee, I will chair the meeting until Dr. Malmud arrives. And then, following the discussion of each agenda item, the chair -- either myself or Dr. Malmud, at our option -- may entertain comments or questions from members of the public who are participating with us today.

Our first agenda item following these opening remarks, we will hear from Dr. Charles Miller, to whom this committee reports, and Charlie will share some -- some views with us.

Charlie?

DR. MILLER: Thank you, Tom. Good morning and welcome, everyone. It's going to be warm in Washington today. I think it's supposed to get up to 88 degrees.

Angela, I don't know if we can get someone to see -- is it warm in here? Are people feeling warm? Comfortable? Warm? Maybe we could see if the building could readjust the conditioning. Absent that, I invite anyone, if you want to take your coat off, please do so. We want to be comfortable in this environment.

This is the first time we've had the meeting in this facility. It's a new facility, and we strive to have it in the ACRS room, but there was a conflict with the room today. I just want to let you know that I've had some meetings with John Larkins. John is the Staff Manager that really runs the ACRS. And John feels that we can -- we can get that room, but I think what we have to do is the same as the ACRS and ACNW does.

We're going to have to be able to schedule ahead when we want to have the meetings. And if we -- if we get dates locked in that don't conflict with the ACRS and ACNW meetings, which are held on the same week every month, I think that we can do a better job of getting that room. But absent that, I think we've got a reasonable facility here today.

I just wanted to take a moment to also apologize on behalf of the Commission for having to move the Commission meeting until this afternoon. It was originally scheduled for this morning. That was kind of beyond our control and the Commission's control.

Two Commissioners were summoned down to Congress this morning and have to appear down there. And what we thought it would be best to have is that when you meet with the Commission you're able to meet with a full complement with the Commission, especially in light of the fact that the two new Commissioners were the ones that were summoned downtown.

So it will give you an opportunity this afternoon to -- to meet with the whole Commission, all five, and it's been a while since we've had five Commissioners. And I'm sure they're very interested in hearing your remarks.

I want to -- I just want to give a note of appreciation for the work that we've been doing over the past year. I think we've made some significant accomplishments, and I think you've made some significant accomplishments helping us. We'll have the opportunity to discuss some of those this afternoon with the Commission, so I look forward to that discussion.

Given the fact, Tom, that we're running a little bit behind, let's move on with the agenda.

Again, welcome.

MR. ESSIG: Okay. We have set aside some time this morning to -- to go over the Commission briefing preparation. We have set that -- some time aside until 9:00. The presentations that the three of you will be doing -- Jeff Williamson has two, and Dr. Eggli and Dr. Vetter each -- each have one.

And I believe at this point -- I mean, the slides are -- have been given to the Commission, so they're -- we really can't change what -- the content. And so I think it's -- we could probably use our time best by just quickly rolling through the slides.

And if anybody has any -- although we can't change the content of the slides, we can certainly, if we need to emphasize some points or --

or deemphasize some points, we can certainly do that. So I think it would be helpful to have the -- any members of the committee who feel that a certain emphasis or deemphasis should be made, that we can do that during the course of the presentation.

I would offer that three of the four areas that we'll be talking about represent works that have already been completed by the committee. They are basically in -- in the past, and, of course, that would be the -- the ICRP recommendations, which Dr. Vetter will be presenting, and the St. Joseph Mercy Hospital case that Dr. Williamson will be presenting. And then, the other one that -- the fourth one -- or the third one, I'm sorry, is the training and experience criteria that Dr. Eggli will be presenting.

All of -- those three are -- as I mentioned, those are completed efforts of the committee, and we thought it would be appropriate that when we were asked for topics this year that we -- we share with the Commission some of the -- or that the committee felt it appropriate, through Dr. Malmud, to share with the Commission efforts that had been completed.

And then, one of them, the medical events criteria, is a work in progress. And the only -- the

only note -- well, on all of these presentations I would emphasize that if there is some -- particularly, I'll just highlight, for example, on the training and experience, the Commission has voted. The rule is final. It's been published, and the committee offered its views to the Commission.

The views of the agreement states were also offered on the number of hours of training and experience, and the Commission elected to choose the option for -- that the agreement states offered for the authorized user training.

And so as I mentioned to Dr. Eggli previously, this is not the time to -- to present to the Commission that -- I mean, you can walk through the process that was used to present -- to formulate the recommendations, and merely note that you had -- you had the opportunity to present the recommendations of the Commission, but it won't serve any purpose if you attempt to tell the Commission that -- that they've made an error and it should rethink the issue. I mean, they voted on it knowing full well -- having the benefit of your -- of your views.

And, likewise, on the Medical Events Subcommittee, that is a work in progress. We don't have yet agreement amongst the subcommittee or the

full committee. But we thought enough progress had been made that it would be worth sharing with the Commission. And I notice in Dr. Williamson's slides that there are some recommendations, and we have to be careful because these are not recommendations to the Commission. They are recommendations from the subcommittee to the full committee.

So I think, Dr. Williamson, as part of your opening remarks, or when you -- when you come to the point in the slide when you say recommendation, make sure that the Commission understands that it's an internal committee recommendation to itself.

MEMBER WILLIAMSON: I will.

MR. ESSIG: And so, with that, maybe we should -- we should go ahead and -- what is the first one that you have up there, Ivelisse? The first one would be -- that is training and experience, I believe. No, I'm sorry. That's the --

MEMBER WILLIAMSON: Tom, I would recommend that --

MR. ESSIG: That's the medical event.

MEMBER WILLIAMSON: -- we not review the medical events slides at this time, but use whatever time savings we can to see if we can get our subcommittee consensus reestablished, because the

presentation I will make to this group is very quick, because it is essentially equivalent the one I had for the Commission staff.

MR. ESSIG: Okay.

MEMBER WILLIAMSON: Because I think a major issue for that presentation is whether we have even a subcommittee consensus at this time.

MR. ESSIG: Okay.

MEMBER EGGLI: Mr. Chairman?

MR. ESSIG: Yes.

MEMBER EGGLI: The iodine incidence will not take its allotted full hour. So if this discussion needs to roll over --

MR. ESSIG: Okay.

MEMBER EGGLI: -- the iodine incidence could easily be done in 30 minutes.

MR. ESSIG: That's good to know. Thank you.

Okay. So the first one that we have for the Commission meeting this afternoon would be the Part 35 training and experience rule, and that would be Dr. Eggli. So if we can -- if we can call up that presentation. Oh, the cap is -- oh.

(Pause.)

All right. I would suggest while we're

trying to -- while we're trying to work out difficulties, we may have a corrupted file.

MEMBER EGGLI: Okay.

MR. ESSIG: We have hard copy of your slides.

MEMBER EGGLI: Actually, they're not in everybody's binder. Apparently, somebody put them in your binder. My binder -- I have my copy, but they're not in the actual binder that was distributed.

MR. ESSIG: Okay.

MEMBER EGGLI: But I can -- we can go ahead. I mean, they were distributed in advance to all the members.

MR. ESSIG: Yes. Why don't we go ahead.

MEMBER EGGLI: Okay. The presentation to the Commission was designed to review the deliberation process. And as Tom said, even though the decision is -- has already been, you know, made, it was my intention to review the thinking process that led toward the committee's recommendations to the NRC staff.

And as background, as part of the revision of Part 35, ACMUI reviewed the training requirements and experience for authorized users, for authorized nuclear pharmacists, for radiation safety officer, and

for authorized medical physicists.

The goal of ACMUI's recommendations for training and experience requirement was to make the requirement commensurate with the risk. And ACMUI established a subcommittee to review the training and experience requirements and make recommendations to the entire committee. The goal was to make the regulation risk-informed and performance-based rather than proscriptive.

With the formation of the subcommittee, the ACMUI discussion revolved around describing elements of training. Who could provide the training? Who could attest to the adequacy of that training?

The initial recommendations were that -- of the ACMUI were that the certifying board could remain actively involved in the training and certification process. An alternate pathway was described for those individuals whose training and experience did not lead to board certification.

With respect that -- with respect to the training programs, ACMUI recommended that training programs would be responsible for developing a curriculum that would satisfy the broad educational and experience objectives required in the regulation. ACMUI did not recommend a specific time allocation for

individual curriculum components, but, rather -- rather specified that content mastery should be the basis of the performance regulation.

In dealing with the question of who can attest to the mastery of a body of knowledge, ACMUI felt that certifying boards would not be able to actually certify competence, but could attest to mastery of a body of knowledge. And this is typical for certifying boards, is that their programs are designed to deliver a body of knowledge and to document mastery of that body of knowledge.

Certification has medical/legal ramifications that were unacceptable to most of the certification boards. With respect to that attestation, ACMUI recommended that the attestation be performed by training directors, since it was the training director who was responsible for similar attestations of training to the certifying boards.

However, the NRC subsequently determined that the public interest would be better served by requiring an authorized individual, in the case of either the authorized user, the authorized medical physicist, the authorized radiopharmacist, would be the individual who would be in the best position to provide that attestation of mastery of the body of

knowledge.

During the Part 35 rulemaking process, recommendations were offered for training requirements for all of the categories of authorized individual. And the ACMUI's recommendations were largely adopted by the Commission. A proposed rule was published based on ACMUI recommendations for a performance-based regulation.

Subsequently, the organization of agreement states expressed concern over authorized user training and experience for requirements of Subpart 200 and Subpart 300 uses. The concern hinged specifically on the didactic requirement and not the overall number of hours of training. The hour recommendation was 700 hours.

In the rulemaking process, the total hours required for training were reduced from 1,000 hours to 700 hours. The distribution of training hours was a concern for ACMUI, particularly for the Subpart 200 and Subpart 300 uses.

In clinical practice in the United States, 70 percent of clinical and therapeutic nuclear medicine is practiced by diplomats of the American Board of Radiology, and it is their training requirements which most carefully are designed to meet

the NRC requirements. And this is because of competing training demands for diagnostic radiology residency, which is now currently one of the longest residency programs in the country at five years for baseline certification.

And there are 11 content areas that have to be mastered during that training period, so that most radiology residency programs will be tailored to meet the NRC's requirement to develop authorized user status within the training program, but probably not in excess of that requirement.

The American Board of Radiology has indicated that it intends to require training programs to train their trainees to the level of certification for Subpart 300, or therapeutic uses. The concern for ACMUI was that because approximately 20 percent of all radiology residents are not board certified immediately on completion of their training program that training directors will have to train radiology residents to the ultimate pathway requirements in Subpart 300, or the Subpart 390 requirements for the alternate pathway.

Some of the most talented radiologists I personally know did not make their board certification the first time around, and then there would be a

period of a year or more during which these diplomats would be unable to become authorized users, if they were not trained to the alternate pathway requirements. So that the American Board of Radiology will require its training programs to train its diplomats to the Subpart 390 alternate pathway requirements.

In its discussions, ACMUI felt that the 200 hours of didactic requirement for Subpart 300 uses was excessive and recommended a didactic component, which now is defined as classroom and laboratory, of closer to 80 hours.

ACMUI was concerned about a negative impact of 200 hours of requirement, because, again, that would shorten the clinical time spent to approximately 500 hours. And since nuclear medicine is different than most of diagnostic radiology, where nuclear medicine is physiologic rather than anatomic imaging, and nothing else in the radiology residency reinforces that physiologic process, that the time spent in developing clinical competence would be truncated by the -- by the long didactic requirement.

There is also potentially a cost associated with the additional didactic training that will have to be borne by the training programs. And

in the current medical environment, those costs are not compensated.

The components of didactic and classroom training are not well defined, and that was the initial intent of ACMUI in its recommendation, that when a program was performance based that it is the responsibility of the training programs to define their programs.

However, as the requirement becomes more defined and less performance based, it becomes more important to define what didactic or classroom and laboratory training actually is. Dorland's Medical Dictionary defines didactic as conveying instructions by lectures and books rather than by practice.

As a result, there will be some potential for misunderstanding of the intent of the requirement, and training directors need to be certain that the programs they design will meet the requirement of the regulation.

And as a result of our further discussion with NRC staff, we would ask that -- that these requirements be defined adequately so that training directors do not have uncertainty about what elements of a training program will be accepted to meet the Subpart 200 requirements and which training components

will not be.

As a person who has to design such training programs, this is of critical importance to me. I do not want to send a preceptor statement forward to later discover that the 200-hour training program that I designed for my trainees was not adequate. This is an area I think that requires further discussion and some degree of resolution with NRC staff.

Thank you.

MR. ESSIG: Okay. Comments on Dr. Eggli's presentation?

DR. MILLER: I'll kick it off.

MR. ESSIG: Okay.

DR. MILLER: Dr. Eggli, you're making a recommendation that we have further dialogue on basically the guidance that's given. Do you have any -- I would be interested in the committee's thoughts on how we might go about doing it.

MEMBER EGGLI: For this committee, and not in front of the Commissioners, essentially what we've done is we've taken a performance-based regulation and made it proscriptive. And I think that if you're going -- if we're going to make the regulation proscriptive, we need to define the components.

I need to know how many hours of lecture I have to provide, and for what is called laboratory experience what elements comprise laboratory experience. You know, is it -- is it participation in surveying? Is it experience in the hot lab? Is it operation of the instrumentation? On a practical basis, what counts?

And I think -- truthfully, I think you need a detailed list of what counts, so that I know what I need to include, because truthfully it's going to be extremely difficult for me to get to that 200-hour mark in any kind of meaningful fashion.

One of the problems that I have is that radiology residents aren't very interested in nuclear medicine. And the more that I put them out into this practical laboratory experience with stuff that they perceive as busy work, the less likely they are to be fired up by many of the new and interesting things that are happening in the field of nuclear medicine.

So I have to try to design a training program that will hold their interest and yet comply with the letter of the regulation, because I think at this point compliance with the spirit of the regulation is inadequate.

MR. ESSIG: Mr. Lieto?

MEMBER LIETO: I would like to echo Dr. Eggli's comments, and I think one of the things that -- and I don't know if he wants to include this as part of the presentation, if it will have value or not, is the fact, in going from this non-proscriptive performance-based requirement in the regulations that this 200 hours really had never gone out for comment.

It was basically a discussion and recommendation from the ACMUI. So you really never had the opportunity for this to go out to the regulated community it's going to effect for comment. So it's something that -- that I think NRC staff and the NRC needs to be aware of.

And my second comment was, to follow up how this is going to be documented, that Dr. Eggli just brought up, is will those activities that are not NRC regulated activities -- could they be included? And that's why I think now that you've gone to this very proscriptive requirement, we're going to really need to know, in these training programs, you know, what's going to be acceptable and what's not going to be challenged.

MR. ESSIG: Dr. Williamson?

MEMBER WILLIAMSON: And I think in the interest of quality medical education and health care,

you should strive to allow them to include as many meaningful things in this lecture or laboratory format as they can, and not force them to spend 200 hours on how to survey a box of equivalent things that -- you know, to -- you know, to overemphasize anyway relatively straightforward technical matters and allow them to be able to include other things such as probably case presentations and other areas -- other topics where the technical and clinical kind of blend together.

MR. ESSIG: Dr. Eggli?

MEMBER EGGLI: And, again, if we look at the -- the requirements for education and training for the more limited uses, which include radioiodine therapy by people who are only doing radioiodine therapy, the requirement for didactic and classroom training is significantly less.

So what we are doing, in part, the Part 300 uses, is we are making a different requirement ostensibly to cover the same material that requires a much lower requirement if all I do is that alone. And it seems if all I'm doing is that alone, you know, the risk to the public is no different if I do iodine therapy in isolation or if I do iodine therapy in conjunction with other radionuclide

therapies and clinical nuclear medicine.

So we've got a -- a double standard here in regulation that I think is a real problem.

MR. ESSIG: Other comments?

MS. SCHWARZ: Sally Schwarz.

MR. ESSIG: Sally?

MS. SCHWARZ: I would like to make one additional comment. Dr. Siegel is very concerned about the number of hours increasing from 80 to 200. And just specifically, you know, the amount of what exactly is going to be added, just as is being mentioned both by Jeff and by Doug, that it would be helpful to exactly know what can be included to increase that training to 200 hours. And cost effectively it's going to be problematic to be able to come to those hours and not take away from the clinical training, if you're adding that much into the didactic coursework.

MR. ESSIG: Okay. Thank you.

Dr. Eggli?

MEMBER EGGLI: One last comment. My concern is we're going to turn out physicians who are well trained in safety and inadequately trained for clinical practice.

MR. ESSIG: Okay. Other comments?

All right. We'll move on to the next topic, then. Oops. I'm sorry.

DR. MILLER: Before we do, I think that we -- you know, I think we need to establish some kind of path forward. The Commission has decided on the regulation. You're bringing concerns to the table that you've aired before that I assume that you will air with the Commission this afternoon.

MEMBER EGGLI: I won't present to the Commission anything more than I did in the formal presentation.

DR. MILLER: Okay. But I think, from my perspective, we need to hammer this out, you know, and I just throw this out as a thought process. I think a way to do that would be to have the committee engaged with the staff in trying to determine what regulatory guidance and what it should look like.

That said, what I think we also need to do, we need to get the agreement states engaged again, because they were big voices in -- in the determination and the Commission -- weighing in the Commission's decision.

While there's representation on the committee from the states, unfortunately Mr. Bailey couldn't be here today. But I'm just interested in

your thoughts on that. I mean, it would seem to me, you know, it means a spirited dialogue. It means a lot of negotiation, and it means, you know, getting the parties to the table to try to hammer it out if we're going to get there with regard to guidance, because the devil sometimes is in the details.

MR. ESSIG: I think Mr. Lieto was first, and then Dr. Eggli.

MEMBER LIETO: Well, I agree that I think the guidance is going to be the next battleground, if you will, on implementation of this training and education.

One thing that I'm a little bothered by is that when we had the discussion, both in the teleconference and I think in a subsequent meeting, my impression -- and it was, again, my opinion -- is that the 200 hours was not a problem with the agreement -- was really an issue with only a couple agreement states that wanted this, and that generally from Mr. Bailey my impression was that the agreement states did not have a problem with our recommendation.

So there has been I think some dynamics that have gone on that this committee is not aware of to get an understanding of why we're at this -- you know, this difficulty that we're at right now.

So I think I agree that we have to have the agreement states, but I -- involved, but I think there also needs to be some understanding that when the agreement states are having input it needs to be understood that the input that we're getting is going to reflect what the actual overall opinion is of the agreement states, because I don't think that was the case.

MR. ESSIG: Well, I would offer that whenever we have an issue that goes to 33 agreement states, we never have unanimity of views. And we try as we can to -- to work through the OAS Executive Committee, Organizational Agreement States Executive Committee, and they present to us a view which is reasonably a consensus view. But I completely agree that there are a number of states that may have not had a problem with the 80 hours.

And then, there were a number of rather vocal ones that -- that preferred the 200 hours and had a -- and had a basis -- they articulated a basis for it. So I understand how we got where we are, and we'll just have to work on the guidance. As we've said, the devil is in the details, and we'll have to talk about that.

Dr. Eggli, you had comment?

MEMBER EGGLI: I was going to comment something similar to what Ralph had just said, but that, again, it was our understanding from Mr. Bailey that it was specifically two of the 33 agreement states who had a serious problem with this, and that's a very small subset of the total. And it's kind of the tail wagging the dog, in a sense.

And I don't -- you know, there is a serious economic impact here, and there is a serious medical education impact here. And, again, I think that a lot of this discussion happened almost out of sight, and this committee certainly didn't have an opportunity to discuss the recommendation or have any dialogue with the OAS.

And I think maybe a format would be to set up some kind of a -- some kind of an opportunity to have discussion between the ACMUI and the members of the agreement statement organization, so that, one, we can share our concerns with them, they can better understand the impact of the recommendation they have made.

And I'm not sure they fully understand the impact of the recommendation they made on a downstream basis, both economically and educationally. And to see if in the regulatory space, in the guidance space,

then, if we can come up with a reasonable agreement between ACMUI and the agreement states.

I'm certainly willing to have that kind of discussion with the agreement states, and have a good give and take as to what we're really trying to accomplish here, because I know that our goals are the same. I know that we and the agreement states want to achieve the same thing.

We come at it from very different perspectives, and I think it would be very useful for us to fully understand their perspective. And I think it would be very useful for the organization of agreement states to fully understand our perspective and our perceptions of the impact.

MR. ESSIG: Dr. Williamson?

MEMBER WILLIAMSON: Well, I'm wondering if perhaps a working group with the -- the three affected stakeholders, if I might call them that -- NRC, the agreement state representatives, and I think some representatives from the nuclear medicine community who are involved in developing educational standards -- and you have the opportunity for more extensive discussions and the opportunity to provide -- develop some sort of a product or draft guidance that could then be reviewed in more detail here. Maybe that

would be a faster, more appropriate vehicle for this process of reeducation rather than a one-hour session before the ACMUI.

MR. ESSIG: Okay. Thank you.

The record will note that Dr. Malmud has now joined us. I can -- I may relinquish my job as Acting Chair of the ACMUI to him and would ask, Dr. Malmud, that you just reposition the microphone that's in front of Dr. Suleiman, so that you may -- you may use it.

Just so that you know where we are on the agenda, we are going through the Commission briefing preparation, and we've heard from only Dr. Eggli at this point. And next on the -- Dr. Williamson has asked that the medical event reporting issues be -- be done last of the -- for the purposes of this dry run, and that next we could go to Dr. Vetter on his ICRP -- his review for the ICRP 2005 recommendations.

And we have done this at the request of the Advisory Committee on Nuclear Waste. We met, discussed the -- the draft recommendations, and then Dr. Vetter carried the views of this committee forward to a special meeting of the ACMUI.

So, Dr. Vetter?

MEMBER VETTER: Thank you very much.

We discussed this last fall, and then I -- as Tom mentioned, I carried our views forward to a meeting of the ACNW, and what I will be sharing basically is a boiled-down version of that information.

So what I'll be sharing with the Commissioners is that our comments will be limited to items of greatest interest to us. The recommendations are quite extensive, and so we'll be -- we simply don't have time to talk about everything. We'll make no comments about environmental recommendations.

One of the things that -- one of the issues that ICRP has been emphasizing in its reports is the issue of justification -- relative to medical exposure is justification. ICRP takes the view that justification of practice lies mostly with the profession rather than government, and the justification of the procedure falls on the practitioners. And ACMUI agrees with that position.

Restriction -- ICRP spends considerable time talking about the concept of constraints, and in some cases constraints are a fraction of the limit. In other cases, constraints are limited to the dose that's acceptable to an individual person or the most highly exposed person, and that might actually be more

than a limit.

So the discussion of constraints tends to be a little bit confusing. They do, however, state rather clearly that they consider achieving constraints to be an obligation, and that a program that exceeds constraints fails.

And it's ACMUI's point of view that failure -- characterizing exceeding constraints as a failure is very negative -- creates a very negative measure. It could actually be counterproductive, and we think that the use of the word "failure" when characterizing a program should be limited to the limits and not to constraints.

Just an example of the use of a constraint, ICRP recommends that constraint for the fetus of a declared pregnant worker should be one millisievert. In this country currently, we have a limit. It's a limit; it's not a constraint -- a limit of five millisieverts for the fetus of a pregnant worker. That has been in place for many, many years. ACMUI considers that to be safe. It's a very small fraction of the threshold at which developmental effects occur, and the risk of cancer in childhood as a result of this sort of an exposure is very, very small, perhaps negligible or zero.

So we think one millisievert may be an appropriate ALARA goal for some, but it should not be used as a constraint.

Just to try to put this into perspective, typical doses to people working in medicine in a cardiac lab are 10 to 50 millisievert to the badge, but in nuclear medicine it's -- well, it's 10 to 50 millisievert to the badge.

The -- it's very easy to constrain, if you will, the dose to the abdomen of someone in a cardiac lab, because the energy of the radiation is quite low, and a half-millimeter lead equivalent apron takes out 97 percent of the -- attenuates 97 percent of the scattered radiation.

So it's rather easy to keep the doses below five millisievert. In fact, most doses to the abdomen are closer to zero in a cardiac lab.

In nuclear medicine, the doses typically do not exceed five millisievert to personnel. So, consequently, keeping the dose to the abdomen is not difficult. However, in the emerging field of PET, we -- first of all, we're dealing with a very energetic radiation of 511 KEV, which is almost an order of magnitude greater in energy than the typical energy in a cardiac lab. So it's very penetrating. There is

nothing you can do in terms of personal protection -- personal protective equipment to try to reduce the dose to the abdomen.

It basically would require removing the individual from that area if you wanted to reduce the dose. So with typical procedures of tens of millisievert to the badge of someone working in PET, the dose to the abdomen is going to greatly exceed five millisievert. And medical centers are going to have to work hard even now to keep doses to the abdomen less than five millisievert for pregnant workers.

So using a constraint of one would clearly require us to remove people from that working area. There is no accommodation that could be made, and this actually would be very disconcerting for those people who had to be removed, and it would be very difficult for employers.

The ICRP also uses the concept of constraint for public dose limits, and they use this in two different ways, which, again, confuses the issue a little bit. For some members of the public, they actually use a constraint that exceeds the limit. In this case, they say that a few millisievert may be reasonable for some of these cases, but that we should

-- but that regulators should not be rigid in applying that constraint.

So, for example, the NRC limits the radiation exposure to a member of the public to five millisievert when that member of the public could come in contact with a radioactive patient that's been released from a hospital, the most common case being use of radioiodine to treat thyroid cancer.

So the limit that the NRC uses is five millisievert. If we review the NCRP recommendations, they also recommend five millisievert to be used in general, but they also say that this in some cases could be -- up to 50 millisieverts could be allowed if those members of the public are instructed and monitored.

For example, if you have a child who -- or an elderly member of the family who is treated and needs considerable care at home, that those members of the public should be allowed to receive more than five millisievert -- up to 50 -- if they are instructed on how to minimize the radiation exposure and if they are monitored. And the ACMUI considers that to be good guidance.

In another case, the ICRP uses constraints to reduce exposures below the one millisievert limit,

and ACMUI considers this -- the use of the constraint in this case to be very problematic in medicine, and it could result in exorbitant costs -- for example, in the shielding of facilities.

NCRP's position is that a -- they don't use the word "constraint." They describe it more or less as a sublimit. They say that, in general, a sublimit of .25 millisievert should be used when making plans that result in exposure of the public, but that in some cases that should be exceeded, and you could design -- for instance, in the design of medical facilities, you could design those facilities to a limit of one millisievert, if you're using -- if you're designing those facilities in accordance with the NCRP recommendations, because there is considerable conservatism built into that formula.

ACMUI's position on this is that ALARA still works, and we think that programs that use ALARA seriously will keep exposures way below one millisievert to members of the public, and we do not believe that a fraction of the -- a constraint should be built into the regulations to force medical facilities to reduce exposures to individual members of the public even further.

NCRP has recently addressed this issue.

In a position statement that was published in 2004, they reiterate that the limit to members of the public should be one millisievert, that in some cases this could -- this should be increased to five -- and this is to a very small number of people in this country actually, and that would be -- for example, it would be for caregivers of radiation therapy patients, radioiodine patients, for example, and that they also reiterated that the limit could be 50 millisievert in extreme cases, such as a child who had been treated with radioiodine, if the parents or caregivers had been properly trained and monitored.

Now, just to summarize some of the issues relative to these limits that ICRP is recommending, we consider that the limit of one millisievert per term for a pregnant worker to be very, very problematic, especially in emerging modalities where radiation exposures could be -- will be -- are considerably higher than that -- for example, in PET.

We're talking about a very small number of people. We're not talking about large numbers of people where we're trying to effect a limit. So we consider the risk, number one, to be very low to the individual, and the number of individuals to be very low.

ICRP is also recommending a general reduction after they made this recommendation previously, and they are reiterating the recommendation that workers have a limit of 20 millisievert. And we consider this to be problematic for certain areas of medicine, PET being the most notable.

So ACRP -- ACMUI supports the NCRP recommendation and the current NRC annual limit of 50 millisievert.

In conclusion, we find that the proposed constraints are very confusing, and in some areas would be particularly problematic. We also consider that the proposed occupational limits are problematic for some modalities.

Even though the average exposure to the -- or the typical exposure to the average member of the worker population of medicine is a very, very small fraction of the limit, there are a few individuals where we are -- we already crowd that limit, and it's absolutely necessary in order for us to deliver adequate medical care.

CHAIRMAN MALMUD: Thank you.

Are there any comments for Dr. Vetter?

MR. ESSIG: Dr. Malmud, I just had one,

and that is the slides that you were using are -- you have some additional slides beyond those that you had given to us earlier that we had sent to the Commission. So we'll have to have copies of those slides made.

MEMBER VETTER: I'm sorry, I'm confused. Relative to the Commission? The Commission report? I didn't send any additional --

MR. ESSIG: No, I'm sorry. To the presentation for the Commission this afternoon, there were -- you had furnished some slides previously. We had six of them at least that are in the -- that are in the -- the notebook that I have that reflects what -- what went to the Commission. And there are some additional slides, so we'll probably need to get -- we will need to get copies of those -- of those made.

MEMBER VETTER: I don't have -- I'm sorry, I'm way off track. I don't even know what you're talking about. I don't recall sending any additional slides for the Commission. They were edited. The ones I originally sent were edited.

MR. ESSIG: Okay. Well, I can -- I can show you what --

MEMBER VETTER: Yes, okay.

CHAIRMAN MALMUD: Tom, are you requesting

a complete set of these slides?

MR. ESSIG: We will need to have -- because I believe what went to the Commission is what we had been given earlier, which were six slides, and --

CHAIRMAN MALMUD: That which would address the need now is a copy of these slides?

MR. ESSIG: Yes. So we'll --

MEMBER VETTER: My understanding was the slides that I just projected is what was sent to the Commission.

MR. ESSIG: Okay. Then --

MEMBER VETTER: That's my understanding. I could be in error.

MEMBER EGGLI: You're using the set that Angela sent back?

MEMBER VETTER: I'm sorry?

MEMBER EGGLI: You're using the set that Angela sent back?

MEMBER VETTER: I'm using the set that Angela sent to me. There was nothing in my -- our packets on what was --

MEMBER EGGLI: I actually printed what Angela sent you, and what you projected matches.

MEMBER VETTER: Okay.

MR. ESSIG: Then, maybe what I have in this notebook, then, is -- is not truly reflective of what went to the Commission. It was my understanding, so -- there were six of them in there, so maybe there isn't a problem.

CHAIRMAN MALMUD: Who would know?

MR. ESSIG: Angela.

CHAIRMAN MALMUD: Angela. So we'll wait.

MR. ESSIG: She'll be back.

CHAIRMAN MALMUD: Thank you.

Any other items of discussion with Dr. Vetter?

If not, having heard from Dr. Eggli and Dr. Vetter, may we move on to Dr. Williamson.

MEMBER WILLIAMSON: Okay. I guess the -- what you'd like me to do is just rehearse my talk on dose reconstruction. I, first, have a question of clarification. Who was the chair of the Dose Reconstruction Subcommittee?

MR. ESSIG: Dr. Malmud.

MEMBER WILLIAMSON: Okay. So this was -- is in error, then.

MR. ESSIG: Yes. You had asked me, and I had sent an e-mail to you, and I gave you --

MEMBER WILLIAMSON: I didn't get that.

MR. ESSIG: Okay.

MEMBER WILLIAMSON: I sent two versions.

MR. ESSIG: Give me a makeup.

MEMBER WILLIAMSON: All right. Okay.

MR. ESSIG: Yes. You were the -- you did most of the technical work for the -- for the subcommittee, but Dr. Malmud was the -- was the listed chair.

MEMBER WILLIAMSON: All right. Do you wish to correct this slide for them -- for the Commissioners, or what should we do?

MR. ESSIG: We can probably --

CHAIRMAN MALMUD: I don't believe that the slide needs correctly. Dr. Williamson did the vast majority of the work, and I'm more than happy for his name to appear there.

MR. ESSIG: Okay. Fine.

MEMBER WILLIAMSON: Okay. All right. Well, in this presentation, I will give a brief overview of the recommendations in ACMUI's report on dose reconstruction.

Contrary to the first slide, Dr. Leon Malmud was actually chairman of our group.

Our charges were to independently review Region III's dose evaluation for an incident that

occurred at St. Joseph's Hospital in Ann Arbor, Michigan. In addition, we were to review the alternate dose reconstruction methodology published in a letter to the editor by Drs. Marcus and Siegel, and, finally, we also made some general recommendations regarding dose reconstruction for our incidents.

Our full membership is listed here. And, again, I emphasize that Dr. Malmud was the chair.

To briefly review the incident under consideration, nearly 300 millicuries of I-131 was orally administered to a patient who subsequently developed impaired kidney function. The patient's daughter allegedly spent six to 21 hours per day in very close proximity to the patient over a time period of six days.

Region III's estimate of the dose received by the daughter was 15 rem. The Society of Nuclear Medicine report by Drs. Siegel and Marcus basically claimed that this assessment was too conservative by factors of 1.6, 7.1, or 17, depending upon which features of their arguments were invoked.

The next slide -- let's see here, catch up. Can you move it to -- okay. This slide illustrates our methodology. We carefully reviewed the Region III calculations, along with the article

published by Drs. Marcus and Siegel.

You know, in addition, we performed some of our own calculations, including limited Monte Carlo simulations. We interviewed the current St. Joseph's Hospital radiation safety officer, and the Region III inspectors who wrote the report. And, in addition, we reviewed additional documents provided to us by St. Joseph's Hospital.

This slide summarizes our findings. Basically, we felt that the 15 rem dose -- the amount calculated by Region III -- was the most conservative estimate possible that is not totally implausible. We did feel that some more sophisticated techniques, including distance reconstruction, were useful and helped us come to a more realistic interpretation of the measurements.

So the bottom line is is that given the dwell-time scenario -- that is, the amount of time Region III believed the daughter was in close proximity to the mother -- our estimate was nine rem.

I think one of the more interesting features of the cases is that St. Joseph's Hospital disputes Region III's dwell times scenario, basically claiming that portable lead shields were used by the daughter 50 percent of the time. If so, according to

our calculations, this would reduce the deep dose equivalent, or DDE, to four to six rem.

One of our recommendations is -- or conclusions is -- that the inspection report should have acknowledged and justified rejection of the St. Joseph's Hospital scenario.

I need to pay attention to what slide I'm on here. Okay.

The critique by Drs. Siegel and Marcus contains several points, many of which we agree with in general terms. One of their recommendations is is that more sophisticated dose reconstruction tools should be used, such as dose reconstruction.

They also recommend that effective dose equivalent, not deep dose equivalent, should be used as the regulation endpoint. The practical difference between these two measures is is that EDE represents dose average over the body core, whereas deep dose equivalent is approximated by maximum dose to the body core.

However, we felt that the methodologies used in the Siegel/Marcus critique were overly simplistic, so we do not accept their particular factors of 1.7 to 17. The next slide, which you can see in the notes, we list the differences between the

Society of Nuclear Medicine document and our factors. Rather than 4.3 for distance reconstruction, our estimate is 1.5; EDE versus DDE factors, 4 versus 6.8; various other factors, they claim 50 percent we didn't think were correct.

So our general recommendations are is that we agree with the general point of the Siegel/Marcus critique that more sophisticated dose reconstruction tools are indicated when doses are near their regulatory limit, when the licensee disputes the NRC dose reconstruction methodology or scenario, when the plausibility of the dose reconstruction assumptions, using more standard and simple techniques, are suspect, or data are not available to justify them.

Then, you know, I think more sophisticated tools to attempt to reconstruct some of the data are useful. Also, when the usual approximations, such as inverse square law, are suspect, more sophisticated tools are indicated.

Continuing with our recommendations, per document RIS 0304, we agree with Siegel and Marcus that EDE should be used as the dose reconstruction regulatory endpoint for Part 20 compliance in scenarios such as the St. Joseph's Hospital.

For disputed dose reconstructions, EDE or

DDE ranges should be used, and acknowledgement and -- of alternative reconstruction scenarios proposed by the licensee should at least be mentioned and justification contained in the report for dismissing them.

Finally, ACMUI believes it is very important that NRC devise some sort of practical system for exempting caregivers from the 500 millirem limited when -- limited when warranted by humanistic or medical consideration.

Thank you.

CHAIRMAN MALMUD: Thank you, Dr. Williamson.

Are there any comments for Dr. Williamson? May I make one? As I recall, having read all of the documents associated with the incident, the caregiver had been warned or admonished by the then current radiation safety officer at St. Joseph's that she was exposing herself to an excessive burden of radiation, and the caregiver said that that was a risk she was willing to take because it was her mother, and she wanted to be close to her. Do I recall correctly?

MEMBER WILLIAMSON: I believe that is correct, yes.

CHAIRMAN MALMUD: May I, therefore,

suggest that in your very introductory slide that you discuss the issue that you comment that despite warnings and admonitions from the radiation safety officer, the caregiver decided to do that, because that's a critical issue that I believe the committee chair should be aware of, because this is an incident in which a radiation safety officer gave adequate information to the caregiver, and the caregiver made a conscious decision not to adhere to the regulations.

And also, we are told not to use the lead shielding that was provided for her, thereby creating a real management problem for the hospital -- namely, how does one deny a daughter access to a dying mother when the daughter says, "I don't care what the rules are. I'm going to do it anyway"?

MEMBER WILLIAMSON: Yes.

CHAIRMAN MALMUD: So it just might be worthwhile inserting "despite" at --

MEMBER WILLIAMSON: So I will say, "Despite admonitions from the RSO regarding radiation burden and the need to use shields, the daughter consciously rejected these instructions." And I'm on firm ground saying that, Ralph? Okay.

CHAIRMAN MALMUD: Does the rest of the committee agree with the insertion of that comment?

MEMBER WILLIAMSON: I think that that's a very good idea.

CHAIRMAN MALMUD: Thank you.

Any other comments for Dr. Williamson?

MEMBER NAG: I think we should make a comment that the -- we should give a dose guideline. However, is there real harm done to a person if you are exceeding the guideline? Like, for example, when you have a chest X-ray or a barium enema, you are getting a larger exposure than recommended for the general public.

So I think we may want to make that clear -- that if they make this decision, and it is -- a barium enema for health reasons, and here it's for the humanistic reason, we should make that apparent.

CHAIRMAN MALMUD: Yes, Dr. Suleiman?

MEMBER SULEIMAN: I've expressed my opinion I think previously, and I'll reiterate it here. Medical patients are exempt, because the benefit -- and if you go through the drill -- always exceed the nominal radiation risk. Occupational workers, the general public, clearly outside the direct -- they're not direct beneficiaries.

I believe that a caregiver is a member of the family or a very close individual. It really is

a unique category. They shouldn't be lumped together with one group nor the other, and I think the NCRP has guidance that addresses this, the current ICRP has guidance, and so my professional opinion is that doses can be kept reasonable, but you have to be compassionate and make a decision.

So I would be careful about using the term "exempt caregivers." Exempt them from what? Unlimited dose? I think a facility could be negligent if they allowed somebody to receive an extraordinarily high radiation dose, but I think the way the practice is it's not a case, should there be a limit, the question is what should the limit be.

MEMBER WILLIAMSON: Well, I will make a reference to Dr. Vetter's presentation which will tie this recommendation to his presentation. I don't think we should, you know, expend huge time on this presentation, which is past business and now I hope relatively uncontroversial, because we have more controversial matters to discuss. I think we should -- well, I'll put in my last slide and make a reference to Dick's position.

CHAIRMAN MALMUD: Any other comments with reference to this presentation? Then, we'll move on to the next one. Dr. Williamson?

MEMBER WILLIAMSON: The next one. Well, what I would recommend, rather than rehearsing my mission talk, is that we basically proceed to discuss the medical event issue in general. And I can give the presentation I have designed for this group, which is very similar, to -- to start with.

The reason for suggesting that, I think that, you know, it has turned out in recent days what we thought was a subcommittee consensus appears no longer to be a subcommittee consensus. So, you know, I think it just would be more productive for us to spend time figuring out to what extent we do have a consensus, so that I know how to temporize my presentation to the Commission this afternoon.

CHAIRMAN MALMUD: Please present it as you will.

MEMBER WILLIAMSON: Okay. So we want to now go to the slides that I had designed for this group -- not that one, no. The original set of slides that I prepared for the ACMUI. Is that a problem?

MR. ESSIG: They should be on another -- because he submitted them previously.

MEMBER WILLIAMSON: I have them here on this flash drive.

MR. ESSIG: Okay. We have copies of

those, do we not?

CHAIRMAN MALMUD: Dr. Nag?

MEMBER NAG: I have a feeling we are not going to solve the issue in the next 20 minutes or so that we have. It might be better if we go over the slides that will be presented to the Commission, so we can say no, this is not something we should represent, or we should. Otherwise, if we rehash, in 20 minutes we are not going to have any consensus.

CHAIRMAN MALMUD: How many minutes do you think it would take to present this first group of slides that you wish to show, Jeff?

MEMBER WILLIAMSON: Probably about 10 or 15 minutes.

CHAIRMAN MALMUD: Well, perhaps we can compromise and allow Dr. Williamson to present this with a discussion not to exceed 15 minutes of the first set, so that we can move directly into the second set, which will be that which we expect to be presented to the Commission. How does that sound to you? Ralph?

MEMBER LIETO: I would -- I would agree with that. And I was just thinking that maybe, if Jeff is in agreement, that as he goes through the slides just point out this -- which slides would not

be in the Commissioners' presentation. It will give us an idea of what would be expected to be in there.

CHAIRMAN MALMUD: Dr. Diamond?

MEMBER DIAMOND: I was just saying that's an official way to address the issue. If there are certain slides being included or excluded, point those out. It will speed up the process.

CHAIRMAN MALMUD: Dr. Williamson is currently occupied trying to get that presented. So I'll ask him the question as soon as he's free.

MEMBER DIAMOND: Jeff, the suggestion was, as you're going through these -- these slides, just point out to the committee which ones are being included and which ones are not being included.

MEMBER WILLIAMSON: I'll be happy to do that.

CHAIRMAN MALMUD: All right. Dr. Williamson, it was suggested while you were occupied that it might be most efficient for you to present the longer set of slides, just indicating which ones would and would not be presented to the Commission.

MEMBER WILLIAMSON: Okay. I will be very pleased to do that.

CHAIRMAN MALMUD: That would save us the time.

MEMBER WILLIAMSON: Yes.

CHAIRMAN MALMUD: Thank you.

MEMBER WILLIAMSON: Okay. All right. Well, this summarizes our charge, as I understand it. I think this is straightforward. We were to evaluate the appropriateness and justification of the 20 percent threshold in the medical event rule, how best to communicate risk, and per this group we were to focus on the permanent interstitial brachytherapy modality primarily, and identify problems in the current ME rule and some proposed solutions.

So here is the history of our deliberations. We have two closed subcommittee conference calls and two noticed public calls with the entire ACMUI. At the last -- second-to-the-last of these we had a consultant, Dr. Louis Potter, who was very helpful in bringing the group to some consensus at that time, and we developed a set of recommendations to be presented at the ACMUI.

In the last week, Dr. Subir Nag, in response to my request that he develop a draft report, has now indicated he has significant reservations with a few -- with some of the recommendations. So it's not clear what the status of our consensus is anymore.

Okay. So what I was going to do is

basically three things -- review some of the -- some background information in permanent seed brachytherapy for the benefit of the whole group, review the consensus we had achieved to date, and review the issues still under discussion or to be discussed. These slides were, of course, made before receiving Dr. Nag's communication late last week.

Okay. So this illustrates what the procedure looks like for prostate brachytherapy. We are talking about prostate brachytherapy because it is by far and away the most commonly practiced form of permanent seed implant. Indeed, with approximately 40- to 50,000 procedures a year, it now appears to be the most frequently practiced indication for all forms of brachytherapy.

So the basic approach is a trans-rectal ultrasound device is used to dynamically image the prostate, as you can see here in the cross-section of the patient. Rigidly attached to this rectal ultrasound probe is a big template, which is hard to see with the lights on here, has a series of holes that direct needles containing the seeds in a direction that is parallel to the probe.

The probe can take either transfer images as illustrated here, or in some cases longitudinal and

possibly three-dimensional reconstructions. So this illustrates more graphically -- no pun intended -- how the procedure looks. Here is the probe, here is the thick plate. There is a series -- matrix of holes corresponding to these dots, which, when the operator looks at the ultrasound image, illustrate the different positions in which needles can be inserted.

For those of you who have not seen seeds, this is what they look like, approximately a quarter of an inch long.

Okay. With that introduction, I thought it would be helpful to understand the procedure flow, at least the most common form of procedure used. So it's divided into three parts -- preplanning, source placement, and host procedure dose evaluation, which occur at different times.

The preplanning occurs generally one to two weeks or so before the actual procedure, and it consists of basically setting up the patient and performing what is called a TRUS -- trans-rectal ultrasound volume study. So the delivery device is used to obtain images with the grid points shown on them, but no seeds are placed at this time.

The prostate volume and critical anatomy is contoured by the physician. Dosimetry data

prescribed dose are input into a program. Preplanning occurs, dose distributions are reviewed, and the outcome of this procedure is basically the source strength, the number of seeds, the source arrangement -- all the things you need as the basis of a written directive.

So this illustrates what the output of a preplan would look like. You can see that the sources are arranged in a very idealized matrix that can never be realized exactly in practice, and then there is a list of instructions indicating what the sequence of seeds and spacers are to be loaded in each of the needles.

Okay. So continuing on, then, with the chronology of the procedure, the patient comes to treatment. Every effort is made to reproduce the ultrasound probe in the same orientation. Imaging -- under image guidance, then the needles are inserted one by one and retracted, depositing the seeds. And this is kind of an iterative process.

So -- let's back up three slides. There. Thank you.

Okay. This is followed, then, by post-procedure dose evaluation, usually performed by X-ray CT imaging. This can occur zero to five weeks after

the implant, depending upon the practice, patterns, and logistic constraints of the individual practitioner.

Its purpose -- imaging is done, prostate is contoured, and then the dose, as actually delivered, is estimated. And, you know, at this point, then, in the conventional practice the written directive could be completed.

So the seed insertion procedure -- a number of things can happen. It's very difficult to reproduce the anatomy of the patient. The prostate may be deformed and displaced. It may be smaller, for example. Seed needle insertion causes prostate swelling. There may be needle insertion constraints which were not appreciated during the preplan.

The bottom line is is that the authorized user must be forced -- must be free to adapt the preplan to the anatomy as actually imaged during the procedure, which can differ significantly from the preplanned anatomy, upon which the original written directive was based.

This illustrates what a post-procedure dose evaluation looks like on CT. You can see the seeds are much more irregularly placed, indicating, you know, the difficulties in literally executing the

preplan. And this is probably a reasonably well-done implant.

I'll say this -- the post-implant doses -- for example, the dose covering 90 percent of the target volume -- are viewed by the community as the most definitive estimate of delivered dose, and this is the endpoint that would be entered into at multi-institutional clinical trials, for example.

So moving on to the medical event definition, the current medical event definition states, "A medical event equals an administration in which the delivered versus the prescribed dose differ by 50 rem and 20 percent, or dose to an extra target site that wasn't planned, exceeds the planned dose by 50 rem and 50 percent." These are the two rules, and this is the -- where we started our critique.

So the first question is: is the 20 percent level justifiable? For temporary implants, the -- let me emphasize, these are recommendations of the subcommittee to the full ACMUI. They have not yet been acted upon by the ACMUI, or transmitted to the staff in the form of a formal report. So this represents an update.

For temporary implants, the group felt that 20 percent is a reasonable regulatory action

level, only if it is understood as a QA performance indicator, not as a patient harm index. For permanent implants, the belief is is, no, this is not appropriate. In many situations, the 20 percent threshold is comparable to the variations encountered in routine clinical practice.

For this reason, in general, we feel that the dose-based medical event definition really is not workable for prostate implants, and I'll go into the reasons a little more.

The rationale is basically that the variability in post-implant CT versus written directive dose comparisons encounter several difficulties. It's based upon different imaging modalities -- preplanning and interoperative placement is based on ultrasound, whereas post-planning is based on X-ray CT.

The literature documents that there can be up to 50 percent differences in the volume of the structures on these two imaging modalities due to the limited soft tissue contrast of X-ray CT. There are large operator-to-operator CT contouring variations as a result of not being able to clearly see the boundary of the prostate on X-ray CT.

There is a long and variable interval from

the time the implant is made to the time a dose is calculated based on post-planning. Then, of course, there are the legitimate preplan modifications that I mentioned. So all of these add up to a significant likelihood of there being a discrepancy close to 20 percent on post-planning versus the written directive, which is based upon the preplan.

Other permanent implant issues is the written directive definition for all other brachytherapy is -- currently allows the authorized user to specify the number of sources and dose, or, equivalently, total source strength, at any time post-implant, and this is because the rule basically defines the -- requires the authorized user to complete the written directive only after the dose is delivered, which in the case of a permanent implant is essentially forever.

Another problem is the wrong site medical event, which the subcommittee believes is unenforceable. The problem is is that small errors in seed position can introduce big dose changes to dose volumes. So there are always -- probably in any implant there is at least some small bit of tissue where the 50 percent and 50 rem threshold is exceeded, if you compare the preplan to the post-procedure plan.

And, finally, to cover the target, it is necessary to implant, on occasion, seeds in normal periprostatic tissue, which may not be reflected in the preplan. And this is not a mistake. This is a legitimate adaptation to the situation that the radiation oncologist finds at the time.

MEMBER NAG: And while you have that slide, I think I need to make a comment. The previous slide. yes.

The Rule 35.40(b)(6) -- actually, it does not allow an authorized user to make a decision. The decision is to be made before -- before the implant, and you can make an oral directive. And I think I need to make a presentation of my own on this. Otherwise, people have doubt and confusion.

MEMBER WILLIAMSON: Well, I think that -- why don't I finish this, and then we discuss I think the remaining issues. That's the point.

Okay. Moving on, so the proposal, at least as of a week ago, which the subcommittee more or less unanimously agreed upon at that time, was that we would define "medical event" in terms of where the sources are implanted, rather than the dose delivered.

So recommendation 1 was, for permanent implants, require that the written directive specify

the total source strength and number of seeds, in contrast to the current definition, which -- and interpretation which allows either absorbed dose or total source strength to be the specifier.

The second recommendation was to replace both the wrong site and target volume medical event definitions -- this is now only for permanent implants with the following -- medical event occurs if: a) the total source strength implanted exceeds the written directive by 20 percent, or the total source strength implanted in the target volume specifically as opposed to the surrounding tissue deviates by the written directive by more than 20 percent.

So this was intended to cover both wrong site and primary dose delivery error pathways in the current rule. And it allows, essentially, 20 percent wiggle room on placing sources outside the specified target volume, in order to achieve a reasonable dose distribution.

Third recommendation was to amend 35.40(c) and (b)(6) -- I believe that should be (ii) -- to require completion and any revision of the written directive within one working day of source insertion.

What is the rationale for these? The major rationale is is determining the fraction of

seeds in the target is much less variable than comparing doses. This is something that we believe can be done interoperatively with prostate implants using ultrasound visualization that is available at the time, thereby obviating the need to compare two plans based on different imaging modalities that may be separated from one another by many weeks.

The third reason is is that limiting -- the final rationale is is that limiting written directive revisions to a time point of 24 hours reduces the opportunity for abuses -- that is, egregious revisions of the written directive made many months later, whose sole purpose is to avoid reporting the event as a medical event.

The fourth recommendation is is that medical events should be treated strictly as QA performance surrogates and divorced from patient harm.

So the two consequences of this, we believe -- one is is that limit the patient and relatives' reporting requirement to those MEs that involve harm or potential harm to the patient, and simply are not technical errors. Second major point is is to model NRC medical event performance on industry quality assurance practices.

So what is the rationale for this?

Medical event reporting is perceived as an invitation for regulatory burden, negative public exposure, and increased liability. And the current reporting rule places the authorized user in a dilemma when he or she believes that reporting to the patient may be medically contraindicated. Then, the physician is faced by a dilemma of medical need of the patient versus preserving confidentiality of the patient's medical information.

The industry practice is well codified in AAPM and ACR recommendations, but it is based on three rod principles. Errors alone are not grounds for punishment. We want people to report them, so that they can come to light in the system improve.

Error reports are used to improve the overall process. And, thirdly, QA deliberations are not discoverable for the purposes of any form of civil litigation.

Unresolved issues are: should dose calculation errors affecting the source strength written directive be exempt from regulatory review? This is something that is currently covered by the medical event reporting rule and the misadministration rule before it, that essentially whatever technical activities are interposed between the physician's

clinical intent and the final realization or delivery of the treatment are fair game for these regulations.

So a proposal that has yet to be discussed is the following -- is to add to the above recommendations a new medical event pathway that would cover errors made in dose calculation that are limited to preplanning. So, therefore, a medical event could be any calculation error leading to an error in source strength specification ultimately written in the written directive that is greater than 20 percent.

This has the advantage of decoupling it from all of the difficulties of post-implant planning by focusing only on the intellectual process that occurs prior to source delivery.

So other medical event issues include: is the current wrong site medical event criterion workable and justifiable for other types of brachytherapy and external beam treatments? This issue whether it should be dealt with is -- is yet to be discussed.

That concludes my presentation.

MEMBER DIAMOND: So, Jeff, perhaps it would be helpful now to highlight the one or two key issues of potential difference for the committee as a whole?

MEMBER WILLIAMSON: Yes. I -- I can try to summarize. I think that the two main ones are -- is if we were to return to my slide where I had the A and B part of the proposed medical event definition. Dr. Nag rejects having the Part B. He would like medical event to read basically, "A medical event occurs if, and only if, the source strength implanted in the target deviates from the written directive by more than 20 percent."

MEMBER NAG: I propose that we postpone any discussion. I think I need to present before we comment.

Before I start, I would like to, you know, state that we had a subcommittee. The people who were in the subcommittee -- the only one who was working with prostate implant and permanent implant on a day-to-day basis was myself as a physician, and Dr. Williamson as a physicist. The other subcommittee members have not been doing permanent implant.

I felt that I needed to get opinion of practicing radiation oncologists, so I took a copy of the American Board -- I mean, American Brachytherapy Society board meeting to present it at the board to get feedback from 12 people who are doing permanent implant every day.

The other thing I would like to mention is that the American Brachytherapy Society has set up standards for permanent prostate brachytherapy and permanent prostate brachytherapy dosimetry, and I am the chair of both of those committees. I'm also on the committee under ACR that sets up the performance on permanent brachytherapy now. I think -- your comments I think would be in place.

A few things -- although Dr. Williamson said that permanent prostate brachytherapy -- permanent implant is mainly for prostate. Whatever recommendations we make should be applicable to all permanent brachytherapy, because if you make the rule for permanent brachytherapy only because of prostate, and it may not apply to others, then you'll have a major problem for people who are doing implants in other parts other than the prostate.

The second thing is that although Dr. Williamson mentioned only about the preplanned method, there are many methods of doing prostate implant. The majority are slowly shifting from a preplan to an interoperative planning system where all the planning is done in the operating room in real time.

The other significant difference I have is that I went back in the Federal Register to see the

actual wordings of similar things, and I'm going to put those wordings in here, because I think it depends partially on how the wordings are interpreted.

Can we have the next slide?

By the way, Dr. Williamson recommends you are also a member of the subcommittee.

I am going to -- now, in addition to the meeting that we had, Dr. Louis Potter came as an expert consultant, and he was present only for part of the meeting. So really the whole discussion was not held with him being there.

We had the input of expert radiation oncologists on March 24th, which is why many of these things are coming after the report and meeting of the 13th. And I'd like to summarize combined opinion expressed in the subcommittee as well as in the expert radiation oncologist meeting.

Now, right now the written directive, as it states, is that before implantation at the site, the radionuclide and dose, and before completion of the procedure, the nuclei equipment site, number of sources, total source strength, exposure time, or total dose.

Now, this requirement I think appropriate for temporary and removable implants, so I think we

are all in agreement with that. The subcommittee members all agreed with that. The only extra comment that the practicing radiation oncologists want to make that -- is that even in temporary implants there are many places that are doing a source strength base that is milligram radium -- are in written directive. Therefore, we should not exclude a source strength based written directive.

Right now, the way the new rule is made, for all implants it has to be dose based. So this is an extra suggestion that was made by the practicing radiation oncologist.

Next, again, majority of the people felt that the dose-based written directive had some problems in permanent implant, because, number one, theoretically, the implant continued to radiate indefinitely. And, therefore, you cannot define when the procedure needed to be completed.

And the other thing that we will show you, and as Dr. Williamson had mentioned, depends on a lot of factors including the volume, the demand, and so on, and, therefore, the authorized user had less control on the final dose.

You have me as a practicing radiation oncologist -- not how much we are putting in, but what

-- but not what the resultant dose will be. And let's see what happens.

That represents where the prostate volume is on CAT scan. Now, in a normal prostate, even before you do an implant, is A the prostate or B the prostate? We think we know, but we don't, because, as I will show you, in brachytherapy, the top brachytherapists in the country would not agree.

What we had in a meeting about three years ago was to ask the top 10 brachytherapists in the country to draw out the prostate, and we had significant difference. And that difference was increased when you are doing it in a post-implant CT, because in addition to the differences in prostate volume, you have edema and hemorrhage and seed artifact.

So, therefore, any of these circles could be the prostate according to some people.

We had the panel meeting in New York, and what we did was we superimposed the prostate on top of each other. There were, I think, 10 or 12 of us there. And we were all told to draw the prostate. Number one, these are the 10 different circles that were drawn by different radiation oncologists and physicists to indicate the prostate at the base, to

indicate the prostate at the apex, look at the difference.

In the mid-plan that was the least different. In the mid-plan, we somewhat agreed on where the prostate is. And what -- how did that matter? Well, depending on which circle you are drawing, you are going to have variation in the prostate volume for each patient. Number one, let's see the numbers.

Case number one, one patient, the range of volume varied from 41 to 63; number two, from 27 to 39. So even though on the same patient different radiation oncologists are saying that the volume is different, so what? If the volume is different, depending on which contour you are taking, you are going to say that the patient got a different dose.

The isotopes -- the second one is 200 percent. This is 150 percent, and the most outside one is 70 percent. So, therefore, if you do a volume that was smaller, and you will see that the patient -- that same patient got 150 percent dose, where if you had gone a slightly bigger circle you would have had -- it only got less than 80 percent. So, therefore, on the same patient you would have misadministration.

With that, the variation in the D-90 dose,

the target dose normally is 125. Therefore, with the 20 percent deviation, if it's less than 116 or more than 174, you will consider that a medical implant. And here, on that same patient, just see the dose. So it depends on whose volume you are looking at. You are going to call many of these patients medical implant when they are not.

This one entered the group, and basically it said the same thing, that you are going to have variation, that they are going to be called medical implant. And why are these? Because it -- in a normal prostate, it's difficult to say what is prostate, what is the muscle, what is the venous plexus, neurovascular bundle, part of the bladder, and the urogenital diaphragm, how much is due to edema, seed artifact, and volume gain with time, because once you have edema the edema will resolve over the next one month. And depending on when you are drawing the volume, you are going to have a different result.

Therefore, I think we all agreed that we should specify for permanent implant the treatment site, the radionuclide, and the total source strength rather than the dose.

Now, in the Federal Register, 10 CFR 35, it states, "Verbal order can be used to modify written

directive if significant change from preplanning occurs during the brachytherapy procedure."

So, therefore, I think that the misunderstanding that you are allowed to change any time you would like, no, you are only allowed to make the change while you are doing the procedure. It can be a verbal order, and you have up to 48 hours to put that verbal order into writing.

Why? Because when we are doing this, we are scrubbed, we are in the OR, we cannot just sign during our implantation procedure. So the law allows us to revise that procedure verbally while we are doing it, but then to put it in writing within 48 hours.

So I do not know where this 24-hour rule came from, and I do not know where the thing came from that you can revise any time you'd like. If you don't like your implant, a month later you can revise it. I don't see anywhere in the 10 CFR 35 that allows you to do that.

And, therefore, according to 35.40(c), the revised written directive should be signed within 48 hours of the verbal order.

CHAIRMAN MALMUD: Excuse me, Dr. Nag. May I just ask you a question?

MEMBER NAG: Yes, sir.

CHAIRMAN MALMUD: In the treatment of the prostate with brachytherapy, there are three possible dose estimates. One is pre-treatment, one is during treatment, and one is after treatment.

MEMBER NAG: Yes.

CHAIRMAN MALMUD: How is the pre-treatment dose calculated? What's it based upon? A CT? Ultrasound?

MEMBER NAG: In most cases, it is based on the ultrasound. However, some people do it based on CT.

CHAIRMAN MALMUD: Does anyone use any other imaging modality?

MEMBER NAG: MRI.

CHAIRMAN MALMUD: MR. So that the pre-treatment dose may be based upon ultrasound, CT, or MR.

MEMBER NAG: Yes.

CHAIRMAN MALMUD: Of those three, in your opinion, which is the most specific? Accurate?

MEMBER NAG: The most accurate -- if you want, we can show you -- is the MRI. However, the MRI is not widely available. In fact, I know it's available in only one or two centers in the country

that are doing an MRI-based.

CHAIRMAN MALMUD: So if we were presenting this to a group of individuals, educated but not familiar with this subject, we should probably inform them that the -- there are three times at which the dose is estimated. The pre-treatment dose, which is based upon either ultrasound or CT, and in some cases MR, depending upon the imaging modalities available to the radiotherapists at the institution in which the patient is being treated.

Then, during -- the second set of dose estimates is during treatment, and that is measured with ultrasound, with a trans-rectal ultrasound.

MEMBER NAG: In most places, except some places do it with MRI, and a few places do it with CT.

CHAIRMAN MALMUD: During treatment?

MEMBER NAG: During, yes.

CHAIRMAN MALMUD: Let me --

MEMBER NAG: And the other thing is, many places, including myself, do not do a preplan, because we do everything in the OR. You know, there is now a change in implanting which obviates the preplan.

CHAIRMAN MALMUD: And if I may just finish my series of questions. And the third dose estimation is post-treatment, and that's done with what

modalities? Ultrasound again, CT, and MR, or just CT?

MEMBER NAG: In most places it is CT-based. But, again, in some places, they are doing it real-time immediately after on ultrasound or on MRI. So, again, it could be either, but most places CT.

CHAIRMAN MALMUD: So if I -- so informing a well-educated group who is not familiar with prostate brachytherapy, we could say very concisely that, apparently, in most institutions, estimates of the dose are made at three times -- prior to treatment, during treatment, and after treatment.

There are three modalities that can be used at any one of these three times. Most often, the techniques are CT and ultrasound, though MR is becoming used more frequently.

The resolution of MR is superior to that of CT and ultrasound in differentiating the prostate from the adjacent tissues.

MEMBER NAG: Yes.

CHAIRMAN MALMUD: Fair statement?

MEMBER NAG: Yes. Except one other thing is that in many places instead of doing it three different times they're compressing all of the three into one session interoperatively, so that you are doing it before the implant but only a few minutes

before the implant. And in post-plant, instead of doing it hours, you are doing it a few minutes after the implant.

CHAIRMAN MALMUD: So that the current state of the art in the United States is for three measurements -- pre, during, after -- in some institutions all of these are compressed to the treatment time itself. And that there are three different modalities used -- ultrasound, CT, MR -- and these have varying degrees of resolution.

And, therefore, depending upon which modality is used, and which technique is used, there may be significant variations in the dose estimates.

MEMBER NAG: Yes.

CHAIRMAN MALMUD: From institution to institution. And also, within the institution, if the dose estimates are based upon different imaging modalities at different times, not to mention the fact that during the procedure and after the procedure there is some anatomic distortion due to swelling and due to the implants themselves.

MEMBER NAG: Right.

CHAIRMAN MALMUD: Now, if I were sitting there as a novice listening to what I just said, I would say to myself, "Are we really ready to establish

criteria for what is or is not an inappropriate dose?" I mean, we have such variation in practice among outstanding practitioners at leading medical institutions in the United States. Are we ready to establish strict criteria? That is a question which I didn't mean to answer, but --

(Laughter.)

MEMBER DIAMOND: Thank you for that non-rhetorical question. I think the bottom line is that the current definition is not workable. Therefore, if the current definition is not workable, can we go and strive to find a better set of guidance and definitions, realizing how imperfect it may be?

With response to one of the other comments you made, Subir, your comment that we should try and strive for a set of guidelines that encompassed the entire realm of permanent implants, I would say that would be a nice goal but is not necessary in that 99 point something percent of the total permanent interstitial implants performed in the United States are directed towards the prostate.

I think if we could go and find something workable for the prostate, I think that would be very helpful.

MEMBER NAG: I agree with you, except that

if you make a set of guidelines that is only applicable to the prostate, then you exclude people from doing implant in other sites. And what I'm saying is we can very easily make our guidelines such it is applicable to the prostate and for any other permanent implants.

CHAIRMAN MALMUD: Dr. Williamson?

MEMBER WILLIAMSON: Yes, I'd like to make a comment. The intent was, of the current proposal summarized in my slides, for it to be applicable to a broad range of permanent implant sites.

You know, I think all of us on the subcommittee recognize that the prostate is kind of an exception, both by virtue of its frequency, but also the fact that it is the procedure where physicians have the most experience integrating image guidance into the process.

And there are other procedures where this cannot happen, and what constitutes a target volume is much more fuzzy. And, therefore, you know, the enforcement criteria and review criteria have to be commensurate with the level of uncertainty in routine clinical practice and basically adjudicating these regulations.

I wish to make one technical correction to

your summary of Dr. Nag's presentation.

CHAIRMAN MALMUD: Yes.

MEMBER WILLIAMSON: He is right, certainly, that when there is interoperative planning everything is compressed into a short time period. But in the conventional paradigm, there is only two dose calculations usually. There is preplanned dose calculation and a post-planned dose calculation.

Generally speaking, unless you're doing the full-blown interoperative planning, there isn't dynamically updated dose calculation during the procedures. Certainly, one -- some can do that, but it's not part of the minimum standard of practice.

CHAIRMAN MALMUD: So, then, it would be more accurate to say that currently, in the United States, dose estimates are obtained at one of the three times -- pre-treatment, during treatment, or after treatment -- during any one to three of those periods of time. And the modalities used are CT, ultrasound, MR, all of which have different resolutions and different qualities and advantages and disadvantages.

MEMBER WILLIAMSON: Yes.

CHAIRMAN MALMUD: All right. Now, having said that, I have two questions, one coming from Dr.

Diamond's comment, one from Dr. Nag. What's the objection to trying to develop a standard for prostate that may eventually, not immediately, be applicable to other organs? Why must we do it for all rather than just one?

MEMBER NAG: If we cannot -- we are not -- it doesn't apply for permanent prostate -- for permanent implants. If you do your guideline for permanent implant that is applicable only in the prostate, you will then exclude people who are trying to do implant at other sites.

The major difference being that in the prostate you have a specified volume, whereas if you -- if you make your guideline only targeted to the prostate you are going to exclude people who do implants on tumor bed after reception. So the tumor is gone, and you are now trying to implant the tumor bed, and you are going to exclude those. So --

CHAIRMAN MALMUD: Perhaps I didn't express myself well. What I meant to ask is: why couldn't a set of guidelines be established for the prostate with the existing guidelines still applicable to other organs until such time as we first resolve whether or not we can deal with the prostate issue.

It's almost like, well -- excuse me. Mr.

Lieto?

MEMBER LIETO: As a member of the subcommittee, I totally disagree with Dr. Nag and the point he just made, because what we're talking about are reporting requirements. There is nothing that this subcommittee is doing is going to affect the practice of putting implants into other areas.

What we're talking about is simply: when does this need to be reported to the NRC? In other words, so that -- how do we set these guidelines or these levels such that they are not -- such that they can't be enforced, which is the current problem -- one of the current problems that we're facing as a subcommittee right now and trying to be addressed.

So, again, I think we're talking apples and oranges here. There is nothing in this discussion or in the presentation that Jeff made that would affect putting implants into lung tumors or brain tumors or anything else with the --

MEMBER WILLIAMSON: Or tumor beds.

MEMBER NAG: And I would like -- I have a few more slides, and then we can continue with that.

Now, what I'd like -- a written directive for permanent implant would be based on prescribed dose. However, if you do that, then, in the example

we showed you, a dose of less than 116 or more than 174 will be considered a medical implant, whereas it's just a normal variation of satisfactory implants.

There was also a suggestion made to place a single prescribed dose with the dose range for permanent brachytherapy procedure, that instead of saying, you know, 140, it goes from 100 to 150. That was unanimously rejected, so that's not a problem.

Now, appropriateness of the 20 percent criteria -- medical implant results, if the total dose deferred from prescribed dose by 20 percent or more, this 20 percent figure, where did it come from? It came from -- ordinarily from the external beam and the Cobalt-60 administration data.

There was really no evidence-based criteria for returning the 20 percent. It was retained because that is what it was in the prior versions. We really don't know whether the variation of more than 20 percent will cause harm to the patient, because it depends on what site, what modality, what volume was radiated, and what was the dose given to the normal tissue rather than the dose given to the tumor.

For example, you can give double the dose to the tumor. So long as the dose to normal tissue is

not exceeded, you are not going to cause any harm.

The 20 percent criteria, the subcommittee opinion was that 20 percent dose was reasonable, action level for reporting QA significance, for temporary implants, for external beam, and unsealed pharmaceutical administration, so long that the medical implant reporting is not automatically treated as an indicator of potential medical harm, which is what we all agreed upon.

Now, for permanent implant at 20 percent, it is not justifiable, and Dr. Williamson, the way it was stated by the subcommittee, was that to define ME excluding seed migration and patient intervention if total source strength implanted anywhere in the patient exceeds written directive by more than 20 percent, or total source strength implanted in the planned target volume deviates from the written directive by more than 20 percent.

When I presented this to the radiation oncologists, there were significant problems. And what -- the overall feeling is that we can still use the wording that is very similar to that written in the 35 -- 10 CFR 35, and just change a couple of words, so we can say something like this. "The medical implant result, if the total source strength

intent of the dose -- if the total source strength implanted into the treatment site -- we felt just keep the word "at the treatment site" rather than talking about planned target volume, because that can differ between different radiation oncologists.

It deferred from the prescribed source strength by 20 percent or more. And it will not be considered to be a medical implant if the deviation resulted from patient intervention or due to seeds that were implanted in the treatment site but subsequently migrated outside the treatment site.

All locations already in the 10 CFR 35 show instead of trying to make -- by trying to make major changes you make things worse. We said that if you just change those wording to the total source strength, it will apply for permanent implant, and we felt this would be a better way to go than trying to coordinate planned target volume and make the 20 percent or more, because once you say that the dose strength implanted into the treatment site deferred from the prescribed source strength by 20 percent or more, it will include someone who is trying to add more seeds, because you are now adding or you are giving a prescribed -- you are giving a dose that is already 20 percent more. So we felt this would cover

both the implants and make it a lot simpler.

CHAIRMAN MALMUD: Thank you, Dr. Nag.

May I ask the committee a question? Having heard professional disagreement regarding the rewriting or making a recommendation to the NRC, how many of you feel that we are currently prepared to present this to the NRC as a completed document of the ACMUI?

MEMBER NAG: I don't.

MEMBER WILLIAMSON: Who believes that we are ready to make that presentation? Do you, Ralph?

MEMBER LIETO: Well, I -- I want to kind of -- do you want a yes/no?

CHAIRMAN MALMUD: Yes, because we have a meeting this afternoon with the Commission, and they're expecting to hear a report.

MR. ESSIG: But not a completed report. This is one of the four items that was listed as a work in progress. And it seems to me what we're trying to do here is to -- we have an hour and 45 minutes on the agenda tomorrow to discuss this topic.

And we're trying to squeeze everything into this, which I wanted to make the point while I have the microphone, I had a phone call during the presentation that reminded me that the chairman has

instituted a new procedure for presentations. There will be a green, yellow, and red light on the table, and what you want to avoid, of course, is the red light. And you do that by -- we have an hour and a half total

The Commission reserves half of that time -- namely, 45 minutes -- for questions and answers. That leaves, for four presentations, 45 minutes. Dr. Malmud will make some opening remarks, which will maybe be a minute or so. So let's take 44 minutes, divided by four, do the math, you're talking about 10 or 11 minutes.

I believe the only presentation that was close to that was, Dr. Williamson, your dose reconstruction ran about 10 minutes. And, Dr. Vetter, yours took about 15, and, Dr. Eggli, yours took about 15. So we'll have to look at compressing those to -- so we can remain within the chairman's guidelines.

This particular issue, it seems to me, we're going to have to -- the Medical Events Subcommittee, we can acknowledge that there are several issues that are currently still under discussion and don't present them as a -- you know, as a completed activity.

MEMBER WILLIAMSON: I think we have no

choice but to make a presentation.

MR. ESSIG: Yes, we do. We have to present.

MEMBER WILLIAMSON: And I will simply indicate -- make my -- my spoken remarks more general and indicate, you know, areas of general consensus, but that there are many disagreements over details.

MEMBER NAG: My suggestion is that there are a few places where I think everyone agrees. We present those, that these have been agreed by the subcommittee. And then, where there are significant differences, we say, "These areas are under discussion, and a detailed or final presentation will be made later." That's the only way we can do it. Otherwise, we cannot -- in 10 minutes we cannot, you know, discuss all of the objections and disagreement, and so forth.

CHAIRMAN MALMUD: Thank you.

Mr. Lieto?

MEMBER LIETO: Mr. Chairman, I think the presentation that Jeff has accurately reflected, at the time that it was submitted, the subcommittee consensus. And I think it being presented in a context this is a works in progress as stated, and at that time that it was presented to the Commission,

what is the consensus of the committee -- subcommittee?

I think the meeting that Dr. Nag had after this document was submitted, and so forth, with the other agencies or societies may provide some valued input, and so forth, to the subcommittee. But we weren't privy to that. So I -- I would say that -- and maybe the timing I'll leave up to the staff and Jeff to decide, but I think that the presentation, as -- as submitted in our packets, does reflect accurately -- and I'd like to hear from David if he agrees.

MEMBER DIAMOND: What you're saying is correct, and I think Jeff has done a fantastic job on this.

And I congratulate you, Jeff, and I think the way that you outlined your discussion is perfectly appropriate. You will go through the slides as previously submitted, and areas where there needs to be a verbal notation as to some areas of disagreement, I think that's perfectly reasonable.

CHAIRMAN MALMUD: Yes, Dr. Miller?

DR. MILLER: If I could just augment what Tom said, so that you're not surprised when you get there. This new protocol that the chairman has put in

is an attempt to try to continue to put more discipline into the Commission rules, and to allow all parties an equal opportunity.

So you'll see not only the lights on the table; you'll see a clock that's counting down. So you won't be surprised that suddenly a light will turn yellow or red. You'll see the clock winding down, and what will happen will be, hopefully, what the chairman has challenged the Commissioners to do is to be disciplined in letting you do your presentations during your time, and then the Commission is given -- each of the Commissioners are given a certain allotted time to ask questions.

And you'll see the chairman pretty much control that. They'll ask a few questions. They'll go on to the next Commissioner. If time permits, they'll come around and ask more questions.

So with the clock there, it gives you the visual effect of doing that. This is something that the staff has been challenged to do in our presentations with them. And the EDO has challenged us to make sure you stay in the green.

MEMBER WILLIAMSON: So we're each going to be given 10 minutes. Is that the --

DR. MILLER: Well, the total presentation

I assume from what Tom tells me is SECY is given 45 minutes. So the total presentation of all four topics --

MEMBER WILLIAMSON: Okay. So it's going to count from 45 to zero.

DR. MILLER: Yes. So it's -- whether you equally apportion it to 10 minutes or somebody takes 12 and somebody takes 8 --

CHAIRMAN MALMUD: Given the effort that has gone into each of the four presentations, there should be 10 minutes allowed for each presentation. That would be the fairest thing to do.

MEMBER WILLIAMSON: Well, I think it would be helpful, then, if someone from the staff gave us a warning when we're at 10 minutes, then, because it would be very difficult to subtract 37 minutes from 45 to figure out what the clock reads.

MEMBER LIETO: Can you electrify the seats?

(Laughter.)

CHAIRMAN MALMUD: It's kind of like testifying before Congress. It's --

DR. MILLER: I think that this is where this came from. I think the chairman took this from what he saw before Congress, and it's to keep the

Commission meetings in the time limit that was allotted and keep the presentations at a certain level.

CHAIRMAN MALMUD: And those of us who have done that have lived through it. It's not difficult.

DR. MILLER: Yes.

CHAIRMAN MALMUD: What do you think of the critical elements, Jeff, that you'd like to point out to the -- to the committee? Because there's so much material that was covered.

MEMBER WILLIAMSON: The critical elements? What do you mean the "critical elements"?

CHAIRMAN MALMUD: Well, the critical elements of your testimony with regard to the 20 percent reporting threshold.

MEMBER WILLIAMSON: I think, you know, just to reiterate, that's a point of general consensus that it's reasonable. I certainly don't disagree with any of the details Dr. Nag has added. I think what I said in one slide was adequate.

CHAIRMAN MALMUD: Okay. Yes?

MEMBER LIETO: I was just going to make one recommendation for the slides. I think the last two slides are added since the committee/ subcommittees met. I think you had two what I'll call

Dr. Williamson slides. Maybe you might want to not present those, since we have not discussed it with the full committee, or whatever, or those two that are in --

MEMBER WILLIAMSON: Those are two that were made specifically for this group --

MEMBER LIETO: Okay.

MEMBER WILLIAMSON: -- because the intent at the time was to -- this would be a lead into our discussion and to frame issues that we should be discussing. Instead, you know, we're returning to older issues that we thought we had consensus on.

You know, I actually think with a little time at least some of these issues that Dr. Nag has brought up could be dispensed with. Whether it's -- everyone agrees that, you know, the written directive definition and associated regulations should not be so elastic that months and months later an authorized user can revise the written directive.

There is, I don't think, anyone on the subcommittee that disagrees with that. I think we could dispense with the issue of what the words mean by hearing from the appropriate member of the staff or Office of General Counsel to determine whether Dr. Nag's interpretation is correct or not. And then,

that would be a major point that would disappear then.

So I would say, you know, we could use the time we have -- if there is time before the, you know, Commission meeting to continue deliberating these issues, we could probably resolve of them.

CHAIRMAN MALMUD: Thank you.

MR. ESSIG: And, of course, I would add it doesn't have to be resolved before the Commission meeting. Are you talking about -- if you focus on the points where you do have subcommittee consensus, and merely indicate that in some areas there are -- because of some recently introduced information from various sources, the subcommittee hasn't had a chance to consider it yet, and that will be done in future deliberations of the subcommittee.

CHAIRMAN MALMUD: Thank you. Does that complete this discussion?

MR. ESSIG: Yes, it does. And I would just observe, maybe stating the obvious, but we're horribly behind schedule. We had, by previous agreement -- Dr. Eggli had indicated that his presentation, rather than the allotted 60 minutes, would only require 30.

However, we had scheduled a break for around 10:00, and, Mr. Chairman, it's your -- it's

your option. We could take the break now, and then continue with Dr. Eggli after the break.

CHAIRMAN MALMUD: That is an excellent idea, since I think people will work more efficiently if they have a break first. So we'll break now for 15 minutes.

(Whereupon, the proceedings in the foregoing matter went off the record at 10:24 a.m. and went back on the record at 10:44 a.m.)

CHAIRMAN MALMUD: Ladies and gentlemen, if I may, I call you back to the committee table.

We will resume with Dr. Eggli's presentation.

MEMBER EGGLI: Thank you. At the last meeting of the ACMUI, the ACMUI was asked by NRC staff to review the I-131 therapy incidents. ACMUI established a subcommittee which included Ralph Lieto, Sally Schwarz, Richard Vetter, and myself to look at the incidents that were described in our binder at the last meeting.

Next slide please. The charge of the subcommittee was to review the I-131 therapy incidents looking for common themes or systematic problems and to make recommendations to the full ACMUI of any

measures which might further reduce administration incidents.

The materials that we reviewed were the NMED summaries that were available. These were summary descriptions of the events, and details were limited. And the assumption that we made as a subcommittee was that all positive observations were included in the summary, and so that absence of a specific observation indicated that there wasn't a problem or it would have been described.

In reviewing the incidents it became readily clear that the number of therapeutic incidents in the United States every year is small compared to the total amount of radioactive iodine administered for therapeutic purposes. There were fewer than 10 incidents per year, and no institution had more than a single administration error.

And in the positive comments in the description there was no evidence that policies or procedures were inadequate in any of those administrative incidents. As a result it was our conclusion that most of the errors were in fact human errors. They could be categorized as failure to pay attention to details, failure to follow established policies and procedures, and missed communications.

And most of those missed communications were verbal. And in reviewing the incidents the question was raised, did the culture in the institutions where the events occurred permit free communication? And did that allow the staff to question the authorized user?

So that our recommendations reflect an effort to further reduce the human error. And again, it's our impression that these were individual human errors.

And so our recommendations deal with verification procedures. And one of our recommendations is that what could be considered is a patient identification verification procedure and administration procedure similar to the rules required in blood banking which in general requires two people to positively identify the patient and two people to review the dose to be administered, or in the case of blood banking, the unit of blood to be administered, to verify that it's right patient, right dose.

Another recommendation is that verbal orders should probably not be permitted at any step of the process of therapeutic dosage administration. In some of the incidents reported there were verbal orders issued for the ordering of the dose. And once

the dosage appeared on site, the chain that verified those verbal orders was weak.

Additional recommendation to the whole ACMUI is that the dosage should be verified against the written directive prior to administration. Essentially that the individual administering the dose ought to have the written directive in their hand. They ought to verify that the dosage to be administered does match the dosage that was actually ordered.

It would be useful for the therapeutic dosage to be re-verified in a dose calibrator on site. We realize that that's not required by the current rule. But again, if therapeutic administration is considered higher risk, I personally cannot imagine re-verifying the dosage received from a central pharmacy on site, and one of the errors was created by a central pharmacy sending an incorrectly labeled dosage that the site did not re-verify in a dose calibrator.

Another problem is two dosages available on site at the same time. And again, the ability to put the iodine into a dose calibrator to measure the activity to be administered prior to administrator would have prevented that particular error as well.

Another key is communication between the authorized user and the individual administering the doses. And those communication chains need to be strengthened. The administering technologist should review the treatment plan with the authorized user prior to administration.

The combination of those sorts of steps, and the subcommittee's feeling was those steps would strengthen the administration process and reduce the likelihood of errors, because the source of error would be reduced by strengthening communication, strengthening the process, strengthening patient identification.

We would also like to see, when incidents are reported, some more detailed information available. We would like to know what were the causes and contributing factors in not just a description of the incident, because it was hard for us to go backwards and try to put together an analysis of causes and contributing factors.

We would like to know, was the authorized user present at the site? Were multiple dosages available on site that might have led to confusion? Was the dose assayed? What role did verbal orders play in the process?

So a more detailed description of the incidents would be helpful in retrospectively analyzing.

But nonetheless, again, it is the opinion of the subcommittee that human errors were largely responsible. And I think we have a number of simple steps that do not have a dramatic burden on the ability to deliver care that might reduce these incidents.

MEMBER NAG: When you are talking about the treatment plan and written directive, are they not the same thing? In one place you mentioned the treatment plan has to be checked?

MEMBER EGGLI: Right. It's essentially the written directive, yes.

CHAIRMAN MALMUD: Any other questions?

The one point that you make - it relates to the dose calibrator. Every nuclear medicine section has a dose calibrator. There may be some practicing medical specialists who do radioiodine therapy who do not have dose calibrators. I personally can't imagine giving a therapeutic dose of I-131 without checking it personally in a dose calibrator, which is our routine, and your routine as well.

However, we should note that this would create a bit of a program for non-nuclear physicians, non-radiologists who are administering I-131 who may not have dose calibrators currently.

MEMBER EGGLI: I think the feeling of the subcommittee was that the value added by a dose calibrator, and an inexpensive dose calibrator is under $10,000, is easily to justify, given the potential risk to the patient of an incorrectly administered dose.

CHAIRMAN MALMUD: I give it a hearty amen. I agree fully. I think Dr. Williamson had a comment.

MEMBER WILLIAMSON: Yeah, I think just to comment, this is also for brachytherapy, other than high dose brachytherapy and gamma stereotactic, the current regulations for brachytherapy and for nuclear medicine no longer require the users to verify any measurement technique at all, the source strengths, so long as it is a unit dosage.

And you can make a case that the vendor has followed industry standards. So anything that would be a recommendation regarding, on this point, which I have great sympathy for, would require a little change.

CHAIRMAN MALMUD: Dr. Williamson's point

of course is correct, and we're aware of that. We nevertheless, as practicing nuclear physicians, I saw Dr. Schwarz also nodding her head, concerned about giving a therapeutic dose without having checked it personally in a dose calibrator.

I'm sorry, Sally, I spoke for you.

MS. SCHWARZ: That's fine. I certainly agree that the presence of a dose calibrator, certainly in therapy doses makes tremendous sense, and I realize they are not now required. So even in terms of the mistaken - dispensing from a nuclear pharmacy when the dose dispensed was incorrect, there is no way to verify that. And it obviously does occur.

CHAIRMAN MALMUD: Dr. Eggli.

MEMBER EGGLI: Just as an experience statement, in my own practice I require that the dose be measured in a dose calibrator - be less than 10 percent off from the dose that I ordered.

Routinely, doses come from our central radio-pharmacy that do not meet that criteria, and if I did not have a dose calibrator on site I would not be able to know that.

CHAIRMAN MALMUD: Thank you. Any other comments for Dr. Eggli?

If not, we'll move on.

MEMBER LIETO: Where do we go from here? We've got a subcommittee report with recommendations. Does, I mean is this something that should be going on to the Commission? Where do we go with these recommendations?

Because as Sally has pointed out, we may potentially be looking at an issue of rulemaking that we may be suggesting to staff.

CHAIRMAN MALMUD: Does a member of the committee wish to discuss this further? Or do you wish to make this as a motion, Dr. Eggli, from the subcommittee to the committee?

MEMBER EGGLI: This is the subcommittee's recommendation to the whole ACMUI. I think it is up to the group as a whole to determine whether or not to endorse this subcommittee report and send it to NRC staff.

I think that would be the appropriate next step would be for the whole ACMUI to determine whether or not it wants to endorse this subcommittee report and send it to staff.

CHAIRMAN MALMUD: If we accept your report as a motion, is there a second to your motion?

MEMBER LIETO: Second.

CHAIRMAN MALMUD: It's been seconded by

Mr. Lieto.

Is there any further discussion of this motion, which you realize will have some implications, particularly if we are recommending, as most of us do, the use of dose calibrators for all therapeutic doses of I-131?

Dr. Vetter.

MEMBER VETTER: Let me just point out that's just one of the recommendations. One of the major problems the committee had was trying to determine what the real root cause was for these medical events.

And so I think in the spirit of the committee's report we hope that the NRC staff would take a look at NMED and see what can be done to provide more complete information. I think that's one of the major findings of the subcommittee.

CHAIRMAN MALMUD: Thank you for clarifying that and reiterating it.

Dr. Miller.

DR. MILLER: Yes. Dr. Vetter, could I pursue in a little bit? Would the report be specific enough as to what changes in NMED would need to take place? And to get that information, would that require a regulatory change or rulemaking?

MEMBER EGGLI: I think this is information that the staff probably has, and it was reported probably by the state. It just wasn't included in the summary. And the comments that we listed, like, was the AU present? Were multiple dosages present on site? Was the dose assayed on site? Were there verbal orders that confused the issue as opposed to written directives?

Again, I know that - when at least internally when we describe what we call a recordable event, whether it's reportable or not, we maintain that kind of detail. And I know that when we forward any such event to our regional office, that that detail is contained within the report.

So I suspect you have all of the material it takes to do root cause analysis, but that NMED is more of a summary, and it is a subset of the information that the NRC maintains at some level.

So I doubt that you have to do any additional information collecting than you already have. It's just how you save it in your summary.

DR. MILLER: I guess what I'm searching for and following up on that is, when you say you supply that, the question becomes - Tom, I don't know if you know the answer to this - are we getting that

information routinely in the reports that are coming in, based upon the reporting requirements.

CHAIRMAN MALMUD: Dr. Miller, is your question, does it relate to the fact that Dr. Eggli pointed out that there were 10 errors? In no institution did more than one arise. And that each of the 10 can be traced back to human error rather than other elements.

And should there be a form on which these data are reported so that they could be tracked, is that your question?

DR. MILLER: Yeah, I think my question is, Dr. Eggli is recommending that documentation needs to be improved at NMED. But to be able to improve that documentation, we have to have that information reported in all cases.

And I guess what I was searching for is, is that in fact happening? That might be a question that I have to my staff.

CHAIRMAN MALMUD: I think Dr. Vetter might be able to address that.

MEMBER VETTER: I think our answer is, we don't know.

The user is expected to provide that information to the NRC, including root cause. NMED is

such a boiled-down summary that very often we couldn't figure out what the root cause was except that it attributed it to human error. So somewhere in the middle there, the answer should be there, but we really don't know if it is. Because we didn't see the original reports to the NRC.

CHAIRMAN MALMUD: Sally Schwarz.

MS. SCHWARZ: Could I make a suggestion that possibly before we would make the recommendation for a rule change that we could actually have someone from staff if they could gather that information, potentially the forms that were submitted from these institutions, and actually analyze if that information was available before we decide that we need a rule change to require a dose calibrator?

It may be that each of these doses was assayed and for some reason still given incorrectly. We don't really know that there was no dose calibrator on site.

CHAIRMAN MALMUD: Dr. Williamson.

MEMBER WILLIAMSON: I think maybe the issue could be simplified in general along the lines of what Sally has suggested.

Perhaps reconstructing your NMED database might be a rather daunting technical project. The

real problem is that if you expect ACMUI to meaningfully review medical events you're going to have to provide more than human error as the root cause. You're going to have to supply more complete descriptions of the events if you want meaningful feedback as to what should be done.

So really, an alternative. So I think that's really the way the motion should read is that to the various medical event subcommittee NRC should endeavor to supply as complete information as possible regarding these events. And since there are very few, this should not be a major burden to gather that material or provide a list of addresses and a database that people could access themselves. For those of us who don't know how to use Adams and so forth, some effort would have to be made.

CHAIRMAN MALMUD: Dr. Eggli, you were able to determine, your committee was able to determine that these were 10 human errors, each occurring at a different institution.

What was the basis for determining that they were human errors?

MEMBER EGGLI: By the summary descriptions in NMED. Again, the assumption that the subcommittee made was that all pertinent positives were provided in

the NMED summary. And that if specific information was not provided, it probably was not an issue.

To make any analysis that kind of assumption had to be made, was that all pertinent positives were provided in the NMED summary. And in the description of the actual event, the summary descriptions were in fact human error type descriptions.

And with the majority of the subcommittee recommendations, this recommends a process that tightens up the communication failures that may have partially led to the human errors and the patient identification failures that may have led to human errors.

And independent of the data available in NMED, those are probably recommendations that stand as reasonable in any case. The recommendation for a dose calibrator I think stands as a recommendation regardless of any more information that may be in NMED.

The question that Dr. Miller asks is, does NRC in fact have the information that we are asking for? The answer to that is, the only area of uncertainty I think in the subcommittee's report, and I guess what the subcommittee is asking is not

necessarily that the NRC acquire any more information, but to provide, when we're analyzing events, to provide all of the information that the NRC possesses to help in the analysis of the problem.

CHAIRMAN MALMUD: Thank you. Does that address your question, Dr. Miller?

DR. MILLER: Yes.

MR. ESSIG: Dr. Zelac has a clarification.

DR. ZELAC: If I could ask Dr. Eggli, do you happen to recall or know how many of the 10 events occurred in NRC jurisdiction states as compared to agreement states?

MEMBER EGGLI: That information was not provided in NMED as to whether it was an agreement state or an NRC state.

Did the numbering help us on that, Ralph?

MEMBER LIETO: It did reference the state, so, it didn't say it was an agreement state or NRC regulated. But it did indicate the state that the event occurred in.

So my recollection - again, this is just - I don't have the data with me - but I think it was about evenly split in terms of where the reported occurrences were.

DR. ZELAC: The reason I ask is that the

current medical event reporting criteria have a compatibility C level with respect to what is expected from the agreement states in terms of comparison and agreement with ours. But the event itself in terms of what the root cause was, it's clearly an element which is necessary regardless of who is responsible for completing the report.

CHAIRMAN MALMUD: Thank you, Dr. Zelac. Another comment?

DR. HOWE: Yes, this is Dr. Donna-Beth Howe with the NRC.

I just have two quick questions. If I remember the database correctly, we had a number of medical events that were supposed to be I-131 administrations that did not require a directive, but material was given that did require a directive.

Did your subcommittee look into or talk about the issue of how to capture those things where there is no written directive because it wasn't supposed to be, but the material itself would trigger one?

MEMBER EGGLI: I think in most of those cases, essentially, a therapeutic dose was given in lieu of a diagnostic dose. And that is part of where our strong feeling that a dose calibrator needs to be

on site came from because had those doses been put into a dose calibrator, it would have been - it should have triggered somebody that the amount of activity being administered required a written directive.

DR. HOWE: My only other comment is that the NMED database at the bottom has a list of references. And many of those references are inspection reports or letters back and forth to the licensees. So those, I think, are available, although the agreement state data is generally pretty limited.

So I think the access to the data is there in NMED, we just have to pull it out.

MEMBER EGGLI: Probably, and some of this has to do with the limited ability of some of the subcommittee members, myself specifically, to navigate the NRC's website.

CHAIRMAN MALMUD: Are the incidents to which Dr. Howe is referring incidents in which perhaps a dose of I-123 without a written directive was ordered but instead I-131 was given, which does require a written directive and given incorrectly because there was no dose calibrated or checked that it was I-131 rather than I-123?

MEMBER EGGLI: I believe that most of the incidents were the intention to deliver less than 30

microcuries of I-131 rather than an I-123.

CHAIRMAN MALMUD: Thank you.

MEMBER EGGLI: And again, what that had to do with the fact, though, is that a higher dose of iodine was physically present on the site and available to be confused with the lower dose.

CHAIRMAN MALMUD: That clearly would be an instance in which a written directive was not required but a dose of I-131 was given in error. And that would be an incident in which the use of a dose calibrator with documentation of the dose immediately before administration would have detected the problem.

Thank you. Yes?

MEMBER RAIZNER: Really just a question. Does anybody have an idea of what the denominator would be of these 10 events? In other words, it's 10 of what number and what percent?

MEMBER EGGLI: The bottom number is huge, probably well in excess of 10,000.

MEMBER RAIZNER: So 10 in 10,000 --

MEMBER EGGLI: It is small.

MEMBER RAIZNER: Would we be improving - that seems like a very good outcome, rather than a very bad outcome. Not that we shouldn't strive to reduce it. But would requiring calibration, do you

believe we would ever eliminate human error entirely?

CHAIRMAN MALMUD: We have a comment from Dr. Suleiman.

MEMBER SULEIMAN: My experience, and I know FDA's experience, is that medical events are grossly underreported, so when it even surfaces, you can assume that it's probably greater than it is.

We see problems all the time with drugs that have similar sounding names, and they're prescribed just because their names are similar. And they're prescribed incorrectly.

So I think if this sounds logically correct, you know, we shouldn't - I always ask that question, what's the denominator. That came up with the recent Vioxx thing. I said, how many people received this drug? And so you were projecting these deaths.

The point is, they probably happen more frequently than you'd care to admit. So I'm impressed with the committee conclusions.

But I think generally the whole medical event reporting science is extremely soft. The databases are frustratingly not complete, at least that's been my experience.

And so the fact that you've been able to

get some information out of this in a credible consistent way I think is commendable.

CHAIRMAN MALMUD: I think the statistical argument in medicine doesn't really carry much weight. Our real goal is zero tolerance for errors. We recognize we'll never achieve it, but it still is the goal.

The issue of a dose calibrator, for example, is just a one-time capital expenditure. It's not an ongoing investment in personnel, because it's the same personnel just taking one more step. So it's not an extraordinary expense.

And considering the damage that could be done from a large dose of a beta emitter as opposed to a small does of a gamma emitter or even a trivial dose of a beta emitter, it's a worthwhile expense. It only would affect very few departments that currently don't have such a device on hand.

But I think the basic issue is that we try to achieve zero tolerance for medical errors, recognizing that we're all human and errors will occur.

Thank you, Dr. Eggli.

MEMBER EGGLI: Actually, there is a motion.

CHAIRMAN MALMUD: Your motion, which was seconded by Mr. Lieto.

Any further discussion of the motion? All in favor?

MEMBER WILLIAMSON: I have a question.

CHAIRMAN MALMUD: Oh, you do?

MEMBER WILLIAMSON: It's a very broad amorphous motion with about six motions all wrapped up in one. I mean does everybody feel comfortable voting en bloc?

CHAIRMAN MALMUD: Well, I think the motion includes - if I may dare to summarize for you, the motion includes the fact that the 10 errors found all seem to have been human; that one of the recommendations for correction of these is better communication systems and better documentation; two witnesses to administer doses; and the recommendation that departments that are dispensing I-131 in therapeutic doses have a dose calibrator on site.

Is that a good summary?

MEMBER EGGLI: Yes, the specific recommendations are contained on slides 7, 8, 9 and 10. It's a limited number of recommendations.

With the exception of the dose calibrator, we did not think that any of the recommendations

imposed a significant personnel or economic burden on any department, and had a good chance of reducing incidents further.

So since the impact was small, it seemed that these were reasonable steps to take. Admittedly the dose calibrator has an economic impact less than $10,000. I can buy a lot of dose calibrators for one malpractice settlement.

CHAIRMAN MALMUD: Dr. Williamson?

MEMBER WILLIAMSON: Well, perhaps my juridical instincts have been sharpened too much by thinking so much about medical events lately. But I frankly feel uncomfortable voting for this and saying all these things should be made in regulations.

I think to make patient verification procedures similar to blood administrations, that's a recommendation for a rule change. It's both too imprecise and too prescriptive in my mind.

So I actually think, rather than take thoughtless action on this package which isn't well specified enough and implies all sorts of potentially complicated rule changes, I think it needs to be split out in little bits or perhaps rescheduled for more extensive discussion and a more detailed proposal made before I'd feel comfortable supporting all of these en

bloc.

Not that I don't have sympathy, or believe there is not value to the recommendations. But essentially what the meaning of making a recommendation is needs to be spelled out, I think, on a bit by bit basis, and we have to determine what recommendations are supported by existing regulations, which would be best handled by guidance, and so forth.

There are just many practical issues that need to be considered before I think this would be meaningful to the staff.

CHAIRMAN MALMUD: I think you've clearly stated your position.

Dr. Eggli?

MEMBER EGGLI: I would like to agree with the concept of Dr. Williamson, with the exception that this is simply a recommendation for possible action, and that everything that Dr. Williamson describes would be part of the process going forward.

We're making a recommendation that this be considered. And again, part of that process would be determining whether this could be done as guidance, as part of existing regulation, whether new regulation is required.

That's downstream. I think the first step

in this process is this series of recommendations to be considered by staff. We're not recommending regulation. We're recommending that a process be considered.

And I think then that everything that Dr. Williamson correctly states will be part of the downstream effort, once the process starts.

MEMBER WILLIAMSON: Well, I think if you could amend your recommendation to more precisely say we should engage in a future process of considering this in more detail, I could support it.

CHAIRMAN MALMUD: I believe Dr. Van Decker wanted to say something.

MEMBER VAN DECKER: I would agree with Dr. Williamson's last statement.

I guess the point I was going to make is, I don't think that anyone wants to jump the gun by saying we want to reopen rulemaking again, even in pieces, after the experiences we've had going through this, and the whole goal of doing the rulemaking process was to put us in a position where we were flexible enough to do other things, and guidance in other ways, so that that becomes a living document.

I think it's very reasonable to say we've had a thoughtful subcommittee that's thought about

this, has a few recommendations, and we can put this on the table for some further discussions as to how this can happen down the line and leave it at that for now.

CHAIRMAN MALMUD: Thank you.

Dr. Lieto, you had another comment.

MEMBER LIETO: Well, I think actually I'm just going to paraphrase what Dr. Eggli and Dr. Van Decker have said, is that I thought the motion was for the committee to accept the recommendations and proceed further. It's not to recommend regulatory changes as part of the motion.

CHAIRMAN MALMUD: Is that your motion, Dr. Eggli, that the committee accept the report and then take the next step within the committee?

MEMBER EGGLI: It is.

CHAIRMAN MALMUD: With that caveat, will you support the motion as amended, Mr. Lieto?

MEMBER LIETO: So seconded.

CHAIRMAN MALMUD: You second it, and does it now gain your approval, Dr. Williamson?

MEMBER WILLIAMSON: Yes.

CHAIRMAN MALMUD: Good. Dr. Miller.

DR. MILLER: At the risk of negating the approvals here, one of the things that the staff needs

from the committee is the committee's advice. And a recommendation of a subcommittee and a report endorsed by the full committee is certainly something of a step in the right direction.

But ultimately what the staff needs is advice from the committee as to what should be done as a regulator. And I think that's what we're struggling with.

So in framing the motion, in framing what the committee decides from the motion, I think we need to think about that aspect of it crisply.

CHAIRMAN MALMUD: Thank you. I believe that those of us who practice nuclear medicine, Dr. Eggli, Dr. Van Decker, myself, could supply the forms that we're currently using as a working document to see how we actually engage in each of these activities that the committee has recommended.

Because actually we do those things as does Dr. Eggli, as does Dr. Van Decker in the practice of cardiology. So we could supply the actual form.

But I don't believe that it's our responsibility to actually draft the final documentation. So we could prepare that, and I think that the motion on the table as amended by Dr. Eggli in support of Dr. Williamson will bring us to the next

step, which is to prepare such a form, which would certainly take care of the issues of misadministration at the time that the patient receives the dose.

Each of the elements that was presented to us would be covered in this form.

That which would not be covered would be if the I-131 did not come as sodium iodide. If it came as I-131 labeled something else, it would still be a mistake in the central pharmacy, which we wouldn't detect in the dose calibrator, because the dose calibrator is testing the activity not the pharmaceutical.

But the point is that the errors that have been described could be largely dealt with with the forms that are currently on hand.

We'd be happy to engage in that process as a committee, I assume, Dr. Eggli?

MEMBER EGGLI: My other comment is, I don't think anything other than the dose calibrator recommendation requires anything other than guidance for what makes a good safety program to implement. Because I think the rest of it is covered broadly in existing regulation, and guidance helps the end user understand how the Agency will interpret the existing regulation.

And again, with the exception of the dose calibrator, I don't think there is anything in the recommendations that requires new regulation. It may require clearer guidance, but I don't believe that anything other than the dose calibrator would require regulations.

DR. MILLER: I agree with Dr. Malmud's statement that it's not the role of the committee to have to craft regulatory tools, whether it's a regulation, guidance, or some other action.

But I think what the staff needs is the conclusions from the committee with regard to your findings. And I think you're close.

I'm thinking of a lot of things, and I don't know how it would play out, so I'm talking off the top of my head h ere.

With regard to the dose calibrator, I think the staff would have - if the committee feels strongly about that as a body, then the staff has to take that on and say, well, what form do we do this in?

In other words, you don't necessarily go off and write a regulation to address that. It may be that we provide guidance to the industry through some kind of generic communication or something to say,

this is a good practice. Is that enough?

Doing this will help prevent human error and help prevent you getting in a situation where you're in violation of the regulations.

That's kind of where I'm coming from, and just saying, conclusions of the committee, making a recommendation to the staff. If as a result of endorsing the report from the subcommittee, it means that the committee needs to do a little bit of further work to do that, whether that's to supply forms or whatever to staff, that's fine.

CHAIRMAN MALMUD: The skills and talents of the members of this committee can prepare such a document. And I think we could volunteer to do that, from which the Agency could then decide what it wants to do.

DR. MILLER: What would be the appropriate action, and then having the staff frame what that appropriate action is, it seems to me that at that time we could come back to the committee for a discussion and endorsement or committee views on what the proposal is as we go from there.

CHAIRMAN MALMUD: Mr. Essig.

MR. ESSIG: I would ask one question. That is, is there additional documentation, to which

I think Dr. Eggli alluded to, that was not in the NMED summary, that the committee or the subcommittee could use in formulating its recommendation to the staff?

And if so we could certainly furnish that if it's available.

CHAIRMAN MALMUD: Dr. Eggli?

MEMBER EGGLI: If there is more detailed information, it would be useful to look at that to make sure that our assumptions were not in error. If our assumptions were not in error, then our recommendations, I think, as a subcommittee stand.

So I would, I guess, as a personal note, I think that the recommendations of the subcommittee for me, as a practicing nuclear medicine physician, who dispenses literally thousands of doses of treatment doses a year - well, maybe not thousands, hundreds of treatment doses a year - I think these are good practice regardless of what other data turns up in NMED.

But I think it would be useful to know, nonetheless, that the assumptions that we based our recommendation on were valid, and that we did not miss some root cause information where we might have made a better recommendation.

CHAIRMAN MALMUD: Thank you. So the

motion has been moved, seconded, and discussed.

Is there any further discussion? If not, I wish to call the motion. All in favor?

Any opposed?

Any abstentions?

Let the record indicate it carries unanimously. Thank you.

We'll move on to the next agenda item. Dr. Vetter. We're up to the case experience using I-125 seeds as markers.

MR. ESSIG: If I could offer one --

CHAIRMAN MALMUD: Please, Mr. Essig.

MR. ESSIG: -- sort of a preliminary thought before Dr. Vetter starts.

This item, as the committee may recall, we had a presentation during the last meeting of the committee by Mr. Gallaghar from Massachusetts, who is the chair of a workgroup that is implementing pilot project number four from the National Materials Program, which the focus of that pilot four group is to develop guidance for us by NRC and agreement state licensees for using these seeds as markers.

And the purpose of today's briefing, I believe, is for Dr. Vetter to share the experience at the Mayo Clinic. But the one thing I would caution

us to do is to not get out ahead - that this committee should not be getting out ahead of the working of this pilot group number four.

This would be certainly useful information for that committee, and I believe that the next meeting of this committee we will have Mr. Gallaghar back. Unfortunately he couldn't be here at this meeting. But we'll have him back either during the next intervening noticed - publicly noticed conference call or at the next face-to-face meeting of the committee, where we'll dialogue further on this issue, using Dr. Vetter's material as input to that committee.

CHAIRMAN MALMUD: Thank you for bringing that fact forward. We were prepared to move the next step except for the absence of Mr. Gallaghar, and therefore, Dr. Vetter's presentation will be the discussion today, and the next meeting that we have Mr. Gallaghar will be able to make his presentation. And then we'll take it the next step along.

I know that there is external interest in this issue. And we do not wish to be a party to delaying it. However, we must give it a fair hearing.

MEMBER VETTER: Thank you. And thank you, Mr. Essig, for that introduction. After Mr.

Gallaghar's report at our last meeting I volunteered to provide some case experience simply because we didn't have much knowledge of this practice.

And so the only purpose of this presentation is to provide some case experience. It's not to make any recommendations.

First of all I'd like to acknowledge a number of colleagues who actually did all this work. This includes physicists, surgeons, radiologists, and technicians. I won't go through who each of them is.

Now the current standard of practice uses a wire to localize the tumor in breast tissue. The radiologist places that wire in the tumor. And one of the disadvantages of that wire approach is that the radiologist's approach to the tumor, implanting the wire, may be different than the surgeon's preference because the surgeon has to basically follow that wire. And it may not necessarily be the best pathway to conserve breast tissue. So there is that disadvantage.

Another is scheduling conflicts. With the wire localization procedure, the surgery generally has to occur the same day because of the risk of the wire being dislocated. Wire does provide some limits for post-localization mammograms. That is, the wire can sort of get in the way.

There is this worry about wire migration. It's not a huge problem, but it is a risk.

And then there is the risk of infection, although that's pretty low. So the alternative that's being explored by a number of medical centers including Mayo being done in research protocols because it's an off-label use of the I-125 seed, is this use of radioactive seeds, that is Iodine-125 seeds, placing them in the tumor in the place of the wire.

The seed that's used is the standard Iodine-125 seed that's used in therapy, although the amount of activity is very, very low compared to what's implanted in a tumor.

Some advantages are that the radioactive seed localization technique can allow surgery to take place up to five days later, and this minimizes scheduling conflicts between the radiologist and the surgeon.

The radiologist can approach the tumor from any direction, because when he or she finishes, they will simply leave the seed in the tumor, as opposed to a wire, which might be sticking out from any particular direction.

It also facilitates bracketing of the

lesions if you need to use more than one seed, and that does not interfere with any of the post-localization mammograms.

Some other advantages. Cost is a wash, and in surgery to remove - for lumpectomies, they commonly will inject some technetium near the tumor and allow that to be drained by the lymph node so that the surgeon then during surgery can find the first lymph node that's draining the breast and remove that lymph node and determine whether or not the tumor is spreading.

The same equipment can be used to do the sentinel lymph node biopsy as is used for the radioactive seed localization procedure.

This shows that the antoges (phonetic) are very similar, but they are distinct enough that simply changing the discriminators on the instrument allows you to usually detect the seed as opposed to the technetium which, there still would be some residual technetium in the breast.

In this particular case experience, some colleagues studied 200 consecutive patients, they did wire localization on half of them, they did that the same day as surgery, and for the radioactive seed localization technique, 68 percent of them were done

at least one day prior to surgery. So in other words this allowed them to delay surgery at least until the next day.

Then the radiologists were asked to rate the preference of using the radioactive seed localization technique versus the wire localization. Patients were asked to rank comfort and convenience.

This shows the box. You can't see the liner very well, but there is a little red liner in there to shield the seed.

Angela, could I get you to click on that box? There is supposed to be a video here. It's not working. We're going to miss the video.

The video is a short video to show how the needle is actually loaded with the seed. A little bit of bone wax is used to seal the end of the needle. The seed is then emplaced - no, that's all right - the seed is then placed inside the needle. It's followed by the stylat (phonetic), which will later be used to push the seed into the tumor tissue. And this is all done under sterile technique. So we're going to miss that.

This shows an ultrasound of the needle and the seed right on the end of it. Here the seed has been pushed out. And in the next view the needle has

been withdrawn and the seed remains in the tissue.

This shows some radiographs of the same sort of thing.

Post-localization mammogram, a little bit hard to see here - if you look real closely you can see the seed right there in that tumor.

So when the patient gets to surgery, the surgeon uses the probe to locate the seed, and then the tumor is dissected and the specimen is - oops, I'm sorry. Here the surgeon is using the probe to confirm that the seed is in the specimen, so that's done immediately after surgery, right there on the drape. Here is a radiograph of the specimen showing the seed in place, and if you look really carefully here, you can see the seed in this specimen. It's located right there.

So it's a fairly straightforward technique.

So the results of this particular study, there were six radiologists who conducted this study. All six preferred the radioactive seed localization technique. Five of them thought the technique was actually technically easier than placing the wire.

When patients were asked to rank comfort and convenience of the seed they considered the

discomfort to be about the same between the two. After all you're sticking a foreign object into the breast. It can't be very comfortable.

Patients rated the convenience, however, of the radioactive seed localization technique considerably more convenient that the wire localization because they don't have to necessarily come when both the radiologist and the surgeon are available on the same day, and they can allow some flexibility both in their schedule, and in the schedule of the radiologist and the surgeon.

During this study one seed migrated from the site due to a hematoma. It actually migrated into the hematoma. But there was no spontaneous migration of the seeds outside the tumor except in that one case. There were no infections reported.

I'll kind of skip over that. The main thing on the results is, other than convenience and so forth, is looking at the actual results, what advantages does that do for the patient?

Relative to margins being negative on the surgery, with the radioactive seed localization technique, 74 percent of the margins were negative, compared to wire localization where 54 percent were negative. And margins that required re-operation, 90

percent of the seed technique did not require re-operation, 90 of them - whereas 76 on the wire localization. So there were more re-operations for wire localization than there were for the radioactive seed, which is obviously an advantage for everyone.

And I don't know what I did here, but my numbers are missing. But basically, if you take the worst case, which is about 300 microcuries of iodine in a seed and leave that in the breast tumor for five days, you'll deliver a dose to the one centimeter margin of about 20 rads, and of course that decreases as you go out.

Typically they're going to take two or three centimeters, so the dose to the breast is in the neighborhood of a few rads.

With 100 microcuries leaving it for one day, this is 1.2 rads. And this is about .3 rads.

That is in the neighborhood of a mammogram. So if you use a low activity seed, and you do surgery within 24 hours, the dose to the breast tissue is about the same as a mammogram. So we're not talking very large doses here, even though that seed is used normally for therapeutic purposes.

So the conclusions were that the technique, the radioactive seed localization technique

was considered to be easy, it's accurate, it's preferred by radiologists. The seeds can be deployed up to five days prior to surgery, and it's significantly more convenient for the patients.

The technique increased the frequency of negative margins in the first specimen, and decreased the frequency of re-operation - a very significant advantage.

Now we're only talking - this is 200 patients. Mayo has done the seed technique on several hundred patients by now, and nothing has changed that conclusion. But still, several hundred patients is not a large number.

But so far that technique is working out very well for us.

Now a question came up at our meeting last time about the integrity of the seed relative to surgeons and their cutting around the seed. What could happen if they struck that seed with the scalpel?

So I asked one of my assistants, Kelly Classic (phonetic), to do a little experiment and see how difficult it would be to compromise the integrity of one of these seeds if we were cutting in some tissue.

So the objective of the study was to determine the vulnerability of the seed by both scalpel and cautery.

So a little experiment was done studying seeds in various configurations. One was a control. One was an attempt to cut the seed with a scalpel. Another one was to rupture the seed with cautery. And they used typical surgery technique of 15 kilowatts, if that's important to this discussion.

So they did that in pig tissue, and then another experiment they actually put the seeds on the stainless steel plate of the electrocautery, so that if someone was trying to cut the specimen on a hard object, what would that do to the seed?

Now they don't do that, but this was sort of what's the extreme of what might be contemplated, that would be it.

So again, a control, attempt to cut the seed with a scalpel, and attempt to rupture it with cautery.

This shows a dummy seed on a stainless steel plate and cutting it with a scalpel. In addition , live seeds, we took some very old seeds that had been in storage for decay, at a fraction of a microcurie, put them on a stainless steel plate, and

attempted to rupture the seed with electrocautery, and then did leak tests on that.

Results. The scalpel did cut through a dummy seed on stainless steel grounding plate, but it required significant pressure. The technologist who was doing this said he had to push down real hard in order to cut that seed with the scalpel.

With cautery he pushed with similar force. And this is a scanning electron micrograph of that seed. And you can see a little bit of a dent there. Cautery was not able to break the seed, and this was pushing down on a hard surface.

MEMBER WILLIAMSON: Which model seed was it?

MEMBER VETTER: This is the ampo (phonetic) seed.

MEMBER WILLIAMSON: 67 11?

MEMBER VETTER: Or 13? Let's see. 67 11, is that it?

MEMBER NAG: Ampo seed, is that the lymph node one, lymph node seed?

MEMBER VETTER: 67 11. So let's see, so yes, in this case we saw the cautery dented the seed. And in pig tissue neither the scalpel nor the cautery was able to damage the seed. The seed simply moved

around. When you tried to push against it with cautery or push against it with the scalpel, it just moved. And this shows no damage to those seeds.

And then the one study using electrocautery to try to break the seed on a stainless steel plate - this was with a live seed, low activity live seed. First they did a wipe test on it to try to detect any radioactivity on the outside of the seed before and after that study.

And then when they finished they soaked the seed in betadine to try to determine if any activity was leaching out of the surface of that seed. And that also was some background radiation. So there was no activity on the outside of that seed.

So basically the purpose of the presentation was to simply give us some case experience and to address that issue of concern, if a surgeon is cutting and strikes that seed, what does that do to the integrity of the seed? And our conclusions were it did nothing, it did not damage the seed at all.

CHAIRMAN MALMUD: Thank you, Dr. Vetter.

Dr. Nag.

MEMBER NAG: One question and some comments.

How many seeds do you typically put in, one or more than one?

MEMBER VETTER: Typically one, occasionally two, to define the margins. Sometimes if you want to define the margins they'll use two.

MEMBER NAG: If you use more than one, then using the gamma probe would not be particularly helpful unless you are using a gamma probe both on the specimen and on the breast because you may have taken one seed out and not the other.

MEMBER VETTER: Oh, true, they do it in both. They use them both.

MEMBER NAG: Now the comments, we have used radioimmuno-guided brachytherapy techniques, where we used to inject radioactive material - radioactive I-125 before the procedure, and in the OR used the gamma probe to define the margins for implants. This is something I see very useful, that can be very useful.

But you made the comment that the wire localization you can have migration but not with the seed. I'm sorry, I think you are going to have equal migration problems. If you had equal sized wire and equal size seed, both of them can migrate.

So I don't think using the seed can

obviate or can improve on the migration problem. It will improve on the reaction problem, because it's radioactive. You can find out where it is.

MEMBER VETTER: The experience of the radiologists of this study showed that there was no migration of the seed.

MEMBER NAG: Right. But what I'm saying is, if there is no migration of the seed, there should be no migration of the wire. They are both equal in size.

MEMBER VETTER: Let's ask a radiologist.

MEMBER EGGLI: Actually they're not. The wire is a very tiny thin wire. It sticks out of the skin, and most wire migration problems come from inadvertent external manipulation of the wire. And where the seed is completely internalized and the wire is a very fine gauge wire. It is like a 23-gauge wire, so that the size of the seed and the size of the wire are in no way, shape or form comparable.

MEMBER NAG: Okay, then in that case I take it back. Because the way I do my localization in other tumors is to use inactive seed, which is about the same size as the I-125 seed. So the migration problem is the same.

We have done a lot of implants using I-125

active seeds, full activity seeds, in the liver and other organs where we are doing surgery at the same time. And so far we have not noticed any rupture of the seeds. And we have used cautery nearby, although I have told the surgeons not to cauterize directly on the seeds. We haven't noticed any loss of integrity on actual patients with full strength iodine seeds.

CHAIRMAN MALMUD: Dr. Williamson.

MEMBER WILLIAMSON: I have a comment, question, comment. I think as a general comment, it seems like a very intriguing and useful application of the product.

The question is, are these seeds freshly manufactured to have this activity, or are they seeds that the vendor has had for nine months and have decayed in storage?

MEMBER VETTER: They are seeds that are ordered from the manufacturer specifically for this purpose and approved for one-time use. How the manufacturer manufactured them, I don't know. Whether he stored them --

MEMBER WILLIAMSON: Well, I think one issue to think about a little bit, I suspect it might not be a problem with I-125, is that - my guess is the manufacturers are taking all their leftover seeds that

they haven't sold, that have decayed away. And so they're very old from the time of reactor activation.

And I think some thought should be given kind of model by model to the presence of high energy contaminant lines in the spectrum.

I think if the iodine is manufactured in the reactor driven way, probably the primary contaminant is I-126, which would decay away quickly. But palladium seeds, if you were to ever contemplate using those, there is a variety of manufacturing techniques, including both accelerator and reactor produced palladium-103, so there is the potential of higher energy lines.

And this of course would not be a problem for seeds which are relatively quickly used after activation, because overwhelmingly the short-lived palladium would outweigh those.

But when you keep a seed for nine months, what started out as .1 percent contamination level would grow proportionately to the low energy. So I think it's one manufacturing issue that should at least be looked at.

CHAIRMAN MALMUD: Dr. Nag.

MEMBER NAG: Maybe I can address that. The manufacturer of the iodine seed had approached me

about five or six years ago to ask me whether seeds that were made for prostate implant were used for permanent implant only, we use usually slightly higher for external. Breast implant, we use slightly lower activity.

But after that those seeds were being thrown away, and they were asking us whether we could use those seeds for any other activity, like using them as a detector.

And so as far as I know, all of these seeds are seeds that were manufactured for prostate implant, permanent implants.

CHAIRMAN MALMUD: Thank you. May I just ask a question? What's the fate of the seeds, Dr. Vetter, after they are removed? I understand the implantation and the surgical removal. Now the specimen goes to pathology. Do the pathologists dissect out the seed, and is there some tracking of the radioactive seed so that they are disposed of in a fashion which is satisfactory to you?

MEMBER VETTER: Well, recognizing that this is all being done on protocols at this point in time, it's not a standard practice yet.

What we require is that a nuclear medicine technologist deliver the seed to the radiologist, and

that a nuclear medicine technologist be called to surgery to collect the seed. It is actually removed in surgery by the surgeon. So it doesn't go to pathology.

We have, however, educated our pathology lab in the event -- they actually have a detector and they check the specimen as well, in the event somehow it got there.

But for the purposes of this protocol, we do track that seed very carefully. It gets delivered directly to the radiologist. It's picked up from surgery by the nuclear medicine technologist. It's then delivered to radiation safety for storage and decay.

It could be - if it becomes a matter of standard practice it could be delivered back to the manufacturer.

CHAIRMAN MALMUD: The loop is closed. The seed is not lost.

MEMBER DIAMOND: Richard, what is the protocol if the patient for some reason cannot proceed with the planned surgery?

MEMBER VETTER: You would ask that.

No, that's a very good question. And the patients are instructed to stay locally, if they are

from a long distance away. They are instructed to stay in a hotel locally until the day of surgery, and to report on that day.

They are called 24 hours in advance to remind them that they have to come to surgery on the next day. So if a patient decided to leave town, so they would leave town with one seed in their breast. It would be a permanent implant at that point, and I'm not sure what the final dose would be.

We've never had that problem.

MEMBER DIAMOND: My comment was really not towards the patient that absconds, but is really towards the patient that has some inter-current illness and is not medically fit to proceed with surgery. The person has some bleeding disorder, has a cardiac issue, so forth.

MEMBER VETTER: Just to respond quickly, I didn't review the exclusion criteria for these patients on the protocol, but I'm sure they screen them very carefully to be sure they're healthy otherwise.

MEMBER NAG: I think very relevant to this would be permanent implants in the prostate, where the seeds migrate to the lungs, we have done sufficient study. We have published our data, which shows that

one or two seeds, and those are full activity seeds, have not had any detrimental effect on the lung or any other organ they may have migrated to.

So my suspicion is that if it is one seed with such a low activity it would not produce any detrimental effect on the tissue.

CHAIRMAN MALMUD: Thank you, in the interests of time, if there are no more questions we'll move on to Dr. Suleiman's presentation. Is that agreeable?

Mr. Essig.

MR. ESSIG: I would just offer if - we had an hour scheduled for Dr. Suleiman's presentation. We need to allow the committee to have lunch as well. So if we want to go ahead with that, is it possible to condense Dr. Suleiman's presentation?

CHAIRMAN MALMUD: Dr. Suleiman spontaneously offered to reduce his presentation to 30 minutes earlier this morning. So he's ahead of us on that subject.

But I will ask him whether he'd prefer to give his presentation before or after lunch?

MEMBER SULEIMAN: Either way. It doesn't bother me at all.

CHAIRMAN MALMUD: All those in favor of

hearing it now, raise your hand.

All those in favor of having lunch first, raise your hand?

Lunch wins.

(Laughter.)

MEMBER NAG: By one vote.

CHAIRMAN MALMUD: We are adjourned for lunch. Can we reduce it to 45 minutes? Would that be acceptable to everyone? Thank you.

So we will re-congregate here at 12:45.

(Whereupon, the above-entitled matter went off the record.)

CHAIRMAN MALMUD: Good afternoon, everybody. We'll get started with the afternoon session. And it will begin with Dr. Suleiman, whose introductory slide is up on the screen right now.

MEMBER SULEIMAN: Thank you, Dr. Malmud.

FDA had a public meeting on November 16, 2004 to discuss some issues associated with human use using certain types of radiolabeled drugs. And I gave a presentation there regarding the radiation dose issues. And so I thought in the spirit of better communication, I'd give that same presentation here.

I'll discuss it later, but I might as well mention it now. The comment period for the public

meeting ended in January, but we are going to extend it to sometime in July. Because at the same time there was another guidance that was being proposed by FDA that was raised at the advisory committee called an Exploratory IND. And that FAR notice hit the streets either late last week or early this week. So their formal closing period is July 13th. So since the Exploratory IND will have some impact on the Radioactive Drug Research Committee program, we decided to keep the comment period open. So if you have any comments, the comment period is in fact open.

FDA allows research without an investigation on a new drug uncertain situations. Most human research in the United States involving drugs requires application of investigation of a new drug, unless the drug's already been improved. And if there are certain criteria that are met, FDA allows human research to be done to be performed with unapproved drugs, again if certain criteria are met, under this Radioactive Drug Research Committee. And I'll review that briefly. So I'd better get going.

In 1975 when the Nuclear Regulatory was established from the old Atomic Energy Commission, FDA promulgated 21 CFR 361.1, which basically authorized such research. These regulations have been on the

books for 30 years. And the November 16th meeting sort of addressed -- actually, it was called Radioactive Drugs for Certain Research Uses. And so we were sort of looking at all the issues associated with that Committee.

Transcripts of the meeting, all of the presentations are all available on the FDA website. So if you want to see what else was discussed, I would direct you there.

As a brief review without going into detail, provisions of 21 CFR 361.1 allowed research to be done without an IND for research drugs if there are certain pharmacological dose limits met. Specifically we say there shall be do clinically detectable pharmacological effect. There are certain radiation dose limits that have to be met.

The qualifications of the investigator, proper licensing and NRC agreement states to your license, informed consent for subjects, the quality of the drug, protocol, reporting of adverse events and separate approval of the institutional review board associated with the institute.

The only hook here is that the committee has to be approved by FDA and consist of at least five members, one of whom is a nuclear medicine physician,

an expert on drug formulation and a radiation dosimetry expert.

So that's sort of the RDRC program in 30 seconds or less. What I'm going to be discussing right now really are the radiation dose limits.

Why do we need to revisit the dose limits? First off in 1975 when we adopted these, we basically used the NRC's occupational dose limits. Since that period of time there have been constantly changing radiation metrics that are more current. A new concept effective dose has been introduced in the scientific community. There's more scientific data regarding radiation risk. And there are also new human research regulations for institutional review boards, which also have some impact on such research.

Does that bother anybody it's off the screen? But anyway, these are the current dose limits. And these were the then occupational dose limits used by the Nuclear Regulatory Commission

If you look at the slide, you can see that in fact it's a two-tier set of standards. We have a whole body limit and we also have organ specific limits. At the time the feeling was that leukemia or active blood forming organs were a major risk. So we had limits for that.

Lens of the eye basically was a derivative of the occupational dose concept. It was felt that if a worker received the maximum dose on a yearly basis, they'd eventually get a deterministic cataract.

At that time also there was quite a bit of concern regarding hereditary effects with the gonads. We've seen since then that the hereditary issues are much, much less than was felt at that time. And then the other organs were sort of thrown in under a catch-all category.

We also made a differentiation between adults and pediatric research where we said subjects under 18 would receive 10 percent of the adult dose.

Also, since the body doesn't differentiate between the source of radiation, we required that the radiation dose that the human research subject received from associated x-ray procedures associated with the research study would also be included in this dose calculation.

As I said, the rationale for adopting the occupational limits were that an adult is able to make a decision, and we assumed that a risk also applies the same way for an informed subject.

And the other critical thing that sometimes seems to be overlooked but it's clearly

there is that the concept of ALARA -- as low as reasonably achievable -- is specified in the regulation. And that even though some of the people felt that the dose limits were too high at the time, the dose limits were intended as that, as a maximum. But it was felt that medical doses could be kept lower to be consistent with the study.

A review of our files basically showed that organ doses are the limiting constraint, not whole body limits. And in general, though the committees must report to FDA on an annual basis so you would expect that when you self-report and list all your doses, we require that all the doses be calculated, you'd expect general compliance. And I use the word "general," because we still do get some examples of doses that have exceeded the organ limits and they're reported to us. But the Committee didn't apparently review all the doses that were there.

Another reason for the change, and I initially wanted to label this slide as just why there's so much confusion, but this is an extremely brief synopsis of what's transpired over the last 30 years. But when the dose limits for the Radioactive Dose Committee were promulgated, the biological absorbed dose equivalent was rem. In '77 the

International Commission on Radiological Protection promulgated effective dose equivalent. And during this period of time until now we still have the international system of units, SI, sort of looming like an 800 pound gorilla and people still use the old units. We're all guilty of it. But the rads to gray, the rems to sieverts, the curies to becquerels.

In 1991 the NRC to their credit got around to adopting the effective dose equivalent about the same time that the ICRP replaced effective dose equivalent with effective dose. Conceptually these are two very similar concepts. There's less difference between them than there was between the introduction of effective dose equivalent. Effective dose equivalent was based more so on mortality risk, whereas effective dose included more morbidity. But probably when you consider the uncertainty associated with the risk estimates, they're scientifically statistically probably very equivalent.

In '93 the U.S. National Council on Radiologic Protection adopted an effective dose. And last year in 2004 ICRP proposed some modification of effective dose. And here's FDA sitting there with a 30 year old set of doses.

Brief review for effective dose. It's

basically what I call a homogenized metric for radiation risk. And it allows, the real value of it, partial body irradiations like a chest x-ray to be equated to a uniform whole body irradiation. So it allows you to compare doses from a variety of sources.

A caveat is that this was designed as a unit of radiation protection and it really was not intended for scientific studies or epidemiological studies where the specific organ doses really need to be known along with the age and the sex of the individuals. But in order to derive effective dose you really need to know the organ doses. And for research you should know the age and the sex.

To calculate effective dose each individual dose is essentially multiplied by its respective tissue-weighting factor. And the sum of all these is the equivalent to effective dose.

Here, just to show you one of the problems with guidances or regulations, is things change over time and sometimes it takes as long to change the regs to keep up with the science. But you can see back in 1977 the tissue-weighting factors have changed somewhat for the gonads. They've been downgraded. The breast has undergone a dramatic change. And that's because like congressional redistricting, the tissue-

weighting factors have to add to 1.0. So if you give, you have to take away from somebody else. So it's a quasi-political, you know, scientific set of numbers. So that's why you've had some anomalous changes there.

And, in fact, at the public meeting Eric Hall from Columbia actually proposed why doesn't FDA just go ahead with a single, assign a tissue weighting factor of .1. He says these aren't too significant figures anyway, so why not just simplify. So we're going to note that comment.

I also went to an awful lot of effort because the value, the value of effective dose is that you can compare doses from a variety of sources. Using effective, though, for standardize from the second column you can compare the dose in millisieverts for relative risk with other metrics for relative risk with other metrics, such as the standard chest x-ray. I spent most of my career doing studies where we measured the dose patients received from chest x-rays. So anytime somebody compares the standard chest x-ray it would always bother me because I knew they didn't understand what the standard chest examine was. But, in discussing this with individuals and with lay people and lay professionals I said which relative metric do you feel more comfortable with. I

was surprised that the chest x-ray seemed to be more-- even though they didn't know what the dose was from a x-ray, they knew that better than background, which somehow confused people which is what I call equivalent time. And I thought as scientists the fifth column was really my piece of cake. I said here, here's the actual risk. Cancer mortality using the ICRP dose coefficients, you know. One in 10,000, one in a 100,000 or so on. And that seemed to be looked at that least. I mean, people were more concerned about the relative issues.

And I do want to make a point here that these are average doses. Inherent in these numbers is a certain amount of very real variability. Background environmental levels may vary by a factor of two, depending on whether you live in Denver or sea level or whatever. Radiopharmaceutical doses may vary by several factors depending on how much activity is delivered to image the patient faster or inefficiencies in the imaging system.

X-ray doses can also vary as much as an order of magnitude. And some exams, like fluoroscopy can vary by as much as two orders of magnitude, a factor of a 100. But these are relatively credible numbers and gives you a feel here.

The bottom two lines, which was really my bottom line was well where do the RDRC dose limits fit in in this. And here you have the whole body dose limit of 5 rem or 50 millisieverts. And also, as I said, the organ doses are constraining. And so here's the red bone marrow dose as an example. And that was much, much less of a dose.

MEMBER VETTER: Excuse me, Orhan, what was your equivalent time again? What is that?

MEMBER SULEIMAN: Oh, equivalent time is just natural background environmental radiation. So three millisieverts which is 300 millirem from the U.S.. And so I've seen slightly different numbers depending on which report people talk about. But the variability is greater than the reported numbers.

So we formally asked at the meeting are current dose limits for adults for research conducted under 361.1. And if not, what should we use? And should there be different dose limits for different adult age groups?

We then continued the discussion to pediatrics, because there has been some recent legislation encouraging pediatric research. There have been recent regulations addressing pediatric research. So we wanted to address this. And we generated a

similar table here.

And I point out here, because we had some nice examples of the dose of 5, a 10 year old and an adult would receive. Because patient size also has a significant impact on how much dose an individual may receive.

The pediatric issue was multifaceted, because I think it was in 2001 there were new regulations by HHS regarding protection of human subjects and Subpart D for additional safeguards for children in clinical investigations. I will not go into detail here, but there has been quite a bit controversy. Part of it is because these regulations define minimal risk, define greater than minimal risk, define indirect benefit to the subject, but they don't give any numbers. So a minimal risk is defined as the risk associated with daily living. And so what does that mean? And so until -- I understand there's some guidance that may come out, but until they actually come up with some guidance, that's really left up to the interpretation of different people.

Also basically from the life span study we're seeing -- back that up. Can you back up the slide?

From the life span study we also see --

we're validating what we suspected that the atomic bomb survivors, they're living longer. Just like the healthy worker syndrome, it's now called the healthy survivor syndrome. They are living longer, but they do have higher levels of cancer, albeit very low levels. You know, they are showing up with that. There's also a non-cancer risk. And this is still a work in progress. Most of the survivors will probably die in the next 10, 20 years in which we will get more of this information. And so we'll have some science. So it's not zero risk, but it's extremely low risk.

And here I want to thank Dale Preston for sharing, allowing me to use this slide. But you can see, this red line here, the zero to 9 at time of exposure survivors. And they have about two and a half relative risk. And if you come down here to the much older population, it's like one fourth. So you've got about ten to 12 fold difference in sensitivity, you know, for these different age groups.

So if you're doing research and you want to keep the risks the same, should we make an effort to adjust for age. So we asked the same questions for pediatric. It's consistent with the human research regulations; do current dose limits appropriate for pediatrics studies, if not what do you think would be

appropriate? And should we have different pediatric age groups?

So this concludes my formal presentation, which I gave at our November 16th meeting. But during that meeting the public was also made aware that FDA was preparing a parallel guidance called Exploratory IND, which would allow microdose quantities of a drug to be tested first in humans and would potentially eliminate the prohibition of first in humans research under RDRC. We do not allow first in humans to be conducted under this research program.

And so there was concern to extend the comment period for the RDRC public meeting to coincide with the Exploratory IND guidance. So that FR notice which was had published it in January, just got published either early this week or very late last week. And the closing date on that is July 13th. And yesterday I found out our closing date is going to be very close to July 13th, but we don't know what date the lawyers are going to put in. But it's going to be sometime in mid-July, so that people will have the opportunity to read both sets, both the public meeting and the Exploratory IND comment.

And, again, if you go to our FDA website, or an easier way is just to go fda.gov and search

rather than try to the long URL link.

Thank you

CHAIRMAN MALMUD: Thank you. Thank you for the update and the presentation.

Any questions for Dr. Suleiman? Dr. Vetter?

MEMBER VETTER: Correct me if I'm wrong, but I think the RDRC regs already take into account pediatrics. Isn't the limit 500 millirem.

MEMBER SULEIMAN: Yes.

MEMBER VETTER: Okay. So it's 5 rem for adults, 500 for --

MEMBER SULEIMAN: It's ten percent of the adult limit.

MEMBER VETTER: Right.

MEMBER SULEIMAN: Correct.

MEMBER VETTER: Now that actually turns out to be consistent with some very recent guidance from EPA which has stated that they believe that the risk to children is anywhere from three to ten times that of an adult, depending on age category. The risk is higher.

MEMBER SULEIMAN: Yes.

MEMBER VETTER: So in fact it's consistent with EPA's recent findings?

MEMBER SULEIMAN: Well, if we're looking at the same science data, we should be drawing the same conclusions.

MEMBER VETTER: Right. Exactly. Yes. So then the question that comes to my mind is why would we want to change that?

MEMBER SULEIMAN: My concern professionally is that there's no differentiation right now between a neonate and a 17 year old. And the difference between a 17 and 18 year old is tenfold in terms of how much they're allowed to receive.

MEMBER VETTER: Okay. Now you look at the EPA guidance, I think it's from puberty up to 18 it's a factor of three. And below that it's a factor ten. So you actually more conservative in protecting the 17 year old than what the data would suggest you need to be?

MEMBER SULEIMAN: Okay.

MEMBER VETTER: So consequently then, I mean my own personal reaction to that would be that, again, we have adequate protection for the entire pediatric range by being a factor ten lower in the limit.

MEMBER SULEIMAN: I mean, I don't want to comment too much, because we're in an open comment

period. But the pediatric issue, as we debated within FDA, was everybody was lumped together whether they're neonate or 17 year old. And even with adults you have a drop off as people get older

CHAIRMAN MALMUD: So you are suggesting that we may wish to consider a weight-based or age-based sliding scale?

MEMBER SULEIMAN: We wouldn't have asked the question if we weren't considering it. And I think we want to hear what the community has to say and then we'll take those comments into consideration and make a decision

CHAIRMAN MALMUD: Thank you again, Dr. Suleiman.

If we may, we'll move on to the next item on the agenda, which is Dr. Sherbini's presentation on establishing guidance on exceeding dose limits for members of the public.

Dr. Sherbini.

DR. SHERBINI: Thank you. Good afternoon.

This subject came up in last year's meeting. And the discussion was we need to do something to allow some people, members of the public who are taking care of patients in the hospital, to exceed the currently allowable dose limits. And we've

done some work on this, and this is what we have come up with.

Okay. The issue is that the dose limit is 100 millirem under normal conditions. And this can be raised to 500 under certain specified conditions. They can be raised by the authorized user, basically. And on some occasions this limit, even the 500 millirem, for caregivers situation.

Where are the high limits needed? Obviously in hospital settings where radioactive materials are being used and where a member of the public is taking care of a patient or participating in patient care, and the dose required for such care is estimated to be much higher than the allowable dose.

We looked at several options, and one of the options which is the one also recommended by NCRP, is to go up to 5 rem. We didn't like this option partly because the underlying considerations for arriving at the 50 millisievert. does not really conform to the caregiver situation in the hospital.

First of all, the annual dose limit of 5 rem represents an apportioned risk, which is the underlying risk is a lifetime risk and were just simply divided over 50 years. And that represents one of the 50 years. So even that doesn't really represent

a meaningful risk level for a caregiver situation. And also, we felt that the 5 rem would not be needed in a lot of situations, in fact in most situations it would not be needed. The needed dose would probably be less than 5 rem, and we felt that allowing a limit that is much higher than is needed may encourage people to use what is allowed, basically, and there is less care in minimizing the dose.

So for all these reasons we felt this was not a viable option.

We then looked at the guides and also the emergency dose situation limits. And these philosophically correspond much more closely to the caregiver situation. But the down side that the dose is way too high. It's inconceivable or very unlikely that anyone would need 25 rem for a caregiver situation. So we felt this was not an option.

Having eliminated these two options, all that we were left with was to basically let the licensee determine what dose is need, and then tell the NRC is what they need. And the NRC would basically approve it. And that is the option we like best, and that is the option we're recommending to the Commission.

Yes, sir?

MEMBER DIAMOND: Just for clarification, could I ask you to define what a patient caregiver is? Are you talking about a family member taking care of an ill relative? Are you talking about a nurse who is providing specific comfort to a patient? I'm just curious about your definition.

DR. SHERBINI: No. This is basically a special case of a member of the public. This is not an occupational situation. So the --

MEMBER DIAMOND: So a family member, for example?

DR. SHERBINI: Yes, a family member, somebody, a friend; somebody like this who would normally under normal circumstances be considered a member of the public.

MEMBER DIAMOND: And therefore by that definition be considered a one time exposure as opposed to an ongoing thing?

DR. SHERBINI: Yes. Absolutely.

So that's what we're recommending to the Commission.

How would this system work? Somebody at the licensee's facility or some authorized person would decide that they have what we might call a caregiver situation. In other words, they have a

family member who needs to take care of a patient. So this is the condition would be recognized and acknowledged.

The user then would estimate how much dose is needed and the regional office would be contacted to obtain a license amendment for that case.

These things might change a little. For example, the authorization from the regional office may not be for a specific patient or a case-by-case basis, it could be for a license which has been done before. So these things still need to be worked out.

MEMBER DIAMOND: Could you move your microphone just a little?

DR. SHERBINI: Pardon?

MEMBER DIAMOND: Can you move your microphone a little?

DR. SHERBINI: Oh, okay. I'm sorry.

All right. Basically there will be certain, you know, procedures that has to be followed to ensure that the approach is not misused or mishandled. And so the caregiver would be provided instructions, they would sign a consent acknowledging the risk that they are undertaking. They would provide it to dosimetry to measure the dose more accurately than just estimating it from survey data.

The dose, the running dose would be tabulated and the radiation protection staff would keep track of it. If the dose is going to be exceeded from what is authorized, then actually it would have to be taken to raise the limit and the new limit would be established.

What we plan to do is if the Commission approves this approach, we would plan to issue guidance. And the purpose of the guidance would be to make implementing this program, more or less, uniform across regions and also by the agreements.

Yes, sir?

MEMBER DIAMOND: If I may, the way I think of this is sort of analogous to what Dr. Williamson was talking about earlier today where this is a very, very rare situation where for humanistic reasons exemptions are granted to current guidelines. So by definition, to go and ask a licensee to request a specific amendment or to go through the amendment process for an eventuality that may never occur to me is not useful. Instead what I would say is probably within the guidance space would be a discussion that in extraordinary circumstances provided certain key step are met such as the clear cut informed consent documentation by the authorized user, use of formal

dosimetry, attempts to minimize the radiation exposure as much as possible. I think that probably would be sufficient. In my career, I've never had one of these instances, for example, and except for the example that we heard earlier I really can't think of an example of this happening.

DR. SHERBINI: Yes. In answer to your question, first of all, the licensee would not request such an amendment unless they feel they need it. So most licensees would not request such an amendment.

And the other thing is that because it is done outside of the regulations, the amendment is necessary otherwise the licensee would be in violation. Because the regulations still apply. I mean, the limit is still 100 millirem or 500 millirem per year. Even if the circumstances are extraordinary, if the licensee allows a member of the public to exceed that, they're in violation and they would have to be cited. And that's what an amendment is supposed to take care of; to put in the license the fact that the licensee is allowed to do this.

We explored the possibility of changing the regulations so that they would do exactly what you just said. But the people who reviewed this proposal almost unanimously agreed that rulemaking is not

warranted. It's very expensive and the number of cases is very small, and therefore it is not warranted, at least at this time.

Yes, sir?

MEMBER EGGLI: I can foresee this happening in my pediatric thyroid cancer population.

DR. SHERBINI: Yes.

MEMBER EGGLI: Where a parent needs to provide care for the child because the child can't manage an isolation environment and maintain the conditions. But although we have some lead time, we don't have massive lead time. How nimble do you anticipate this system to be to respond to these special situations as they arise?

Sometimes our lead times are a week or two, sometimes they're shorter than that. But they're not months. So how nimble will this kind of system be?

DR. SHERBINI: We are hoping, if we do this right, we are talking days. Not more than days. And if a department, a pediatric department has a need for this kind of thing on a regular basis, it might be possible to put this into license so you don't have to get an amendment for each patient. But that would be a broader --

MEMBER EGGLI: You mean that would be to describe the general case of a parent caring for a child?

DR. SHERBINI: Yes. Absolutely.

Yes, sir

CHAIRMAN MALMUD: I think Dr. Williamson had an earlier question.

DR. SHERBINI: Oh, Dr. Williamson?

MEMBER WILLIAMSON: No. Dr. Eggli essentially asked. My question was I was concerned that the license amendment process could respond in a timely enough fashion to preclude, for example, like the St. Joseph's Hospital event from escalating.

DR. SHERBINI: Yes.

MEMBER WILLIAMSON: Because perhaps sometimes the level of cooperativeness of a relative can't be predicted, and the event might be ongoing. So I should think very nimble.

DR. SHERBINI: Yes. I think the purpose of the guidance is to have everything in place in such a way that once a phone call is received from a licensee, everything would be more or less automatic. It's been worked out before, all the details are worked out before. So it would be a matter of just quick approval. And so it shouldn't take much time at

all.

Yes, sir?

MEMBER VETTER: My question as along the same line. The only experience we've had that is similar to this was with an iridium implant where I received a phone call at 10:00 at night and the patient was going downhill was very fast.

DR. SHERBINI: Yes.

MEMBER VETTER: The family wanted to spend time with the patient. And the patient had to be moved to ICU. And so we were able to provide portable shielding and so forth to accommodate that.

DR. SHERBINI: Right.

MEMBER VETTER: But with widely dispersed radioiodine, it wouldn't be nearly that easy. And so at 10:00 at night I'm going to have to call someone at NRC and say -- I mean, in terms of the response time, that's what we would be looking for.

CHAIRMAN MALMUD: It would be rare occurrence, though, would it not?

MEMBER VETTER: Oh, yes. These are very rare.

DR. SHERBINI: Yes. We would have to work this out. I'm not sure how to answer this question at this point because we haven't worked out the details

yet.

CHAIRMAN MALMUD: Dr. Nag?

MEMBER NAG: We are not frequently, like on and off, in this situation with low dose rate brachytherapy in the pediatric population. We solve it most of the time by using high dose rate so that we don't expose the parents. But I think that we'll be able to solve it a lot of time, we work on a case-by-case basis. Can we not have in the guidance that in a situation where a similar condition exists, you would be able to exceed if it is in a medically -- with all these provisions that you have made that, you know, that the relative be informed and informed of the risk and so on?

DR. SHERBINI: Yes. This can be arranged by simply making the amendment broader than patient-by-patient as I said earlier. Every time you have a patient you call, then it will be your department is authorized to do this for any patients in a similar situation. So that's possible.

CHAIRMAN MALMUD: Yes?

MEMBER RAIZNER: A question. You focused on the caregiver but you mention in the slide higher level may be needed in some hospital settings. Are you referring there to hospital personnel? And that might

be the more common scenario. And would you anticipate a similar system of notification for that one specific individual and that specific situation? That might be a more --

DR. SHERBINI: Well, if we're talking hospital personnel, I would interpret as somebody who is occupationally exposed. And they don't fall into this population.

MEMBER RAIZNER: So they would not need special provision for --

DR. SHERBINI: No, they're already limited to 5 rem per year, so that really isn't a problem.

Yes, sir?

MR. ESSIG: We do have the plan special exposure that is occupational that they can implement.

DR. SHERBINI: I understand that, too. Yes. Right

CHAIRMAN MALMUD: So, Dr. Sherbini -- or, excuse me. Dr. Schwarz?

MEMBER SCHWARZ: I just was asking if like Dick Vetter has suggested, that there's ever been an opportunity in their facility to have an occasion that might be warranted at 10:00 at night, would it be reasonable for these institutions to then automatically -- I mean, at the point the guidance is

written, to go ahead and submit an amendment that would cover at least an initial starting point that would allow that licensee to have a higher limit for these particular cases. Though they're isolated, at least it would avoid that 10:00 at night call if they could anticipate a situation. And then possibly as the case would progress, they might have to then revisit the NRC and ask for another increase in the exposure for that particular person.

DR. SHERBINI: That would seem reasonable. But I don't know if it would be legal. We would have to check with our lawyers to see if we can do that.

Yes, sir

CHAIRMAN MALMUD: Dr. Sherbini, it sounds as if what the Committee is suggesting is that the first element of this be the requirement for contemporaneous notification to the NRC district office that this is a need, allowing the practice of medicine to move forward and giving the NRC office adequate time to respond. Because, in general, if the exposure is going to be significant, it's going to be over a matter of days anyway. So the NRC regional office would have time to respond.

It'll be interesting to review that, as you will do with NRC legal staff, to determine if

that's acceptable currently in the event that another event situation should arise similar to one that occurred in the hospital Michigan.

DR. SHERBINI: Yes. I think for occurrences that transpire during the day, that should not be a problem. And that's the whole purpose of preworking out all the details. But the situation that was raised as to late at night, I'm not sure how this could be handled. We can probably work out something, but I'm not sure how.

CHAIRMAN MALMUD: Dr. Zelac?

DR. ZELAC: It's probably worth noting that if a particular licensee is going to implement a specific procedure where they anticipate that the doses to the caregivers will exceed the current limits, they can apply in advance, as Dr. Sherbini has said, to get an amendment to their license to cover that circumstance.

We have at least one broad scope licensee who has done exactly that and has described both the dose limit that they feel is appropriate for the parents of the children, as well as the training that the parents will receive, as well as the safeguards that they will implement for all the parents. And they have an amendment and can on a routine basis treat

patients following that protocol.

CHAIRMAN MALMUD: Thank you, Dr. Zelac. Dr. Suleiman was next.

MEMBER SULEIMAN: I had a similar comment. First off, to have to file an amendment to allow this seems to me absurd and very difficult. Okay. I would think that any license that's going to administer therapeutic quantities of a drug probably would have in it an inherent -- you know, something to address this sort of situation. And I don't mean particularly anything from Ralph Lieto's presentation, but I was looking at it and I think -- it shouldn't have to be done on a case-by-case basis. I think this has the potential of being done more frequently and maybe just isn't reported as often. But I think making it just part of a license application would be appropriate.

DR. SHERBINI: Well, you know, taking this route involves a lot of work and preparation. And I would imagine that generalizing it to most licensees would be cumbersome for most licensees, because most of the things that need to be done under this method would not be done by most licensees. For example, monitoring, instructions to people who are about to exposed, the caregivers, et cetera. There are a lot of things that you need to do if you're going to do

this, which you wouldn't otherwise. And so generalizing it would really not be beneficial for most people. It would be cumbersome.

CHAIRMAN MALMUD: We're looking forward to the next step in the process as it evolves.

DR. SHERBINI: Thank you. Thank you.

CHAIRMAN MALMUD: Oh, Dr. Miller?

DR. MILLER: Yes. If I may just supplement. It seems to me there's two aspects of this proposal that Dr. Sherbini has made on behalf of the staff. One is the technical merits of what he's proposed. And I think, you know, as we move forward, part of the reason for his presentation today I think is so that the Committee understands where the staff has come out with regard to the technical merits of it. That meaning, should there be an absolute dose limit or not. And I think we've concluded that there shouldn't be. It's a case-by-case basis.

We don't know how the Commission will react to that proposal. But I guess what's beneficial is to know how that strikes the Committee. And I think Sami's had some preliminary discussion with the Committee on this already.

The other side of is is what we'll call the legalistic aspect; how do you implement it? And

the license amendment is the vehicle, but in practice what you're asking for is an exemption to the regulations as they're currently written. And if it's rare that this takes place, our lawyers will entertain exemptions. If we find that it becomes more routine, then what our lawyers instruct us is we can't regulate by exemption; that we have to change the regulations.

And so I think what Sami's proposed I think he feels is something that will happen in a more rare case, if I understand it, so therefore the exemption process would be more appropriate for that.

I recognize what we're also looking for here is your insights, and some of it has already been put on the table concerning the timing of it. Is this something that you're only going to know a few hours in advance? Can it be predicted? Is it something that gives enough time? We have mechanisms in place to move fairly rapidly on emergency actions if the merits of the case meet the action. But if those emergency actions, as I said, become more routine than not, we're pushed by our lawyers to get a permanent regulatory fix to the problem.

So there are the issues that we're going to face as we move forward on this.

CHAIRMAN MALMUD: Thank you, Dr. Miller.

Is there another comment? If not, we'll move on to the next item on the agenda, thanking Dr. Sherbini for -- did I hear who?

MEMBER LIETO: I think I have a presentation on this.

CHAIRMAN MALMUD: Dr. Lieto? You are the next item on the agenda

MEMBER LIETO: Just as background note, I know that these slides are not in the packet, although they were sent out individually to staff and to ACMUI members. But there are also copies, I believe, of the slides on the desk if people have not gotten them yet.

In putting together my presentation, I did not, unfortunately, have the benefit of Dr. Sherbini's slides, so I did though use as some input the draft staff document that ACMUI commented on I think in January that addressed sort of a draft position that NRC staff was looking at regarding this specific subject.

Just as some background as to what the purpose is, the impetus for this, the discussion of the dose reconstruction and the incident that involved that St. Joseph's Hospital in Ann Arbor, which was addressed at the Commissioner's meeting in April of last year. It was further affirmed as a secondary

goal of the dose reconstruction and specifically a goal of the ACMUI at its meeting following that in April.

That should say 2004, not 2002. Sorry about that.

And most of this has been specified in a SECY document 04-0107, which I'll refer to just as SECY 107 in the future.

The issue, as I see it, is that we have dose limits for members of the general public which are either family members or external caregivers that may exceed the 100 millirem annual limit for members of the general public.

We are specifically looking at situations where the hospitalized patient contains a therapeutic amount of radioactive materials. Now, as I understand it, the limit for members of the general public in terms of the documentation for allowing them to get the 500 millirem applies to released patients. Okay. What we're talking about is still hospitalized patients. So it's the 100 millirem limit that is applicable here.

And just to sort of underscore that, that was one of the major violation citations to St. Joseph's Hospital, was exceeding the 100 millirem

limit. Not the 500 millirem.

And what I'm going to present here are a couple of assumptions that I think we've already addressed. These are rare occurrences for any individual licensee. The initiating event can and could occur and did occur in an extremely short period of time, within a matter of 24 hours. And to underscore this point, it occurred over a holiday.

So I think requiring even regional emergent approval of a license amendment would not have satisfied or benefitted this situation that occurred at St. Joseph's.

The licensee has resources available because of existing authorization for hospitalized patients.

Now, the guidelines that I'm going to present here are basically what should that dose limit be on that be members of the public that would be allowed. Who these guidelines should apply to specifically. And a process for that should be incorporated into this or could be incorporated into these guidelines? And where should reference for these guidelines occur in?

I'll take the latter one first. There are different types of references where the guidelines

could be established. One would be in regulation. I think we're all in pretty much agreement, this is really undesirable to have this in a very prescriptive regulatory space as well as the fact just the time to achieve coming to some resolutions on guidelines, we could be looking at years.

A license amendment is still a regulation. It's a de facto commitment. It is a prescriptive requirement. And it is something that the licensee would have to stay on top of as they go about changing this. So that if a license amendment was submitted, say now and was approved and yet this event that might occur years down the road, did occur, heaven forbid, the situation may be such that they may need to make some changes to that. They would have to go back into amendment space, if you will, with the NRC to get changes to that.

The preferences, again from my perspective, would be either as a regulatory guide which is a well established mechanism, or the regulatory issue summary which is a relatively new thing with the NRC. But in reading what is the purpose of a regulatory issue summary, a couple of the objectives for that is to solicit voluntary licensee participation and staff sponsored programs. Another

purpose of this is to announce staff technical or policy positions not previously communicated to licensees or broadly understood. So that might be a more positive mechanism, plus giving us some latitude in changing things as we go along.

Now, there may be another guideline that NRC staff may be familiar with that they might want to present that these guidelines should be in. But I think definitely the former two there, or the first two regulations or license amendments are definitely undesirable.

The next point that I wanted to make a recommendation for discussion is the allowable dose limit. In the draft staff statement or document they basically said let's leave it up to the licensee. The first thing a licensee is going to ask is what limit do you want. Okay. They're going to need some boundaries by which they can act upon in terms of communicating risks and implementing procedures.

I'm recommending a two tiered approach in that there would the 100 millirem to 500 millirem or one to five millisievert which would simply require notification of the NRC regional office and/or the agreement state.

Now I'm kind of questioning this because

I don't know if the agreement states are empowered under their compatibility rules to allow these higher values, if you will, or these differences in the dose limits. Again, I would defer to NRC staff to clarify that. But simply it would require an immediate notification of the situation to the NRC regional office and if appropriately, in the case of an agreement state, to the appropriate agency in the state.

The second tier would be up to 5 rem or 50 millsieverts. Again, same type of notification in addition to fulfilling certain criteria and commitments.

Now, the 5 rem justification is that the 5 rem has been addressed in NCRP Commentary 11, which specifically addressed dose limits to individuals who receive exposure from radionuclide or radiopharmaceutical therapy -- or radionuclide therapy patients.

I do disagree that with Dr. Sherbini that I think in terms of a risk limit, an equivalent risk limit that the fact that 5 rems is being allowed for occupational radiation workers does provide a justification for allowing exposures up to that level. It's again, just simply not from an apportion

standpoint, but just simply the risk to an individual from radiation. And also that 5 rems, even though as Dr. Suleiman has pointed out, this is a fairly old, the FDA still does allow up to 5 rem dose limit for research subjects of agents that are "generally recognized as safe."

So I think the 5 rem is a reasonable justification. And when you look at it as being a factor of 50 larger than what is allowed right now, I think it still allows a very large increase in exposure to a member of the general public. And I think by establishing also a limit, it does provide a justification in trying to maintain an ALARA concept to how much you're going to allow the individual.

Now, who would be the patients that would be involved in this? Obviously, if there was a life-threatening situation where the patient is going to pass away in a matter of hours or days, there's a compassionate implication or reasoning here. As Dr. Eggli brought up in the case of pediatric patients where the medical care might be adversely effected without the family caregivers being present, but it would require determination by the patient's physician and possibly the authorized user. In other words, there would need to be a documentation that both the

referring physician and the authorized user were involved in this situation of allowing for this situation to be occurring.

The family caregivers, I seem to recollect that in NCRP Commentary 11 they actually define what they mean by the caregivers in these types of situations. And it would be essentially, as was discussed earlier, a relative or an extended family member who has been involved with that individual's care.

A suggestion is not including minors or allowing minors to be present. I think there's, obviously, there probably is going to be some discussion on maybe that point. But it's just, again, a suggestion in terms of recommendation of who these caregivers, family caregivers are.

And that it has to be willingly accepted. It can't be something where these individuals are saying they need some additional care, you need to be there. It's got to be something that's willingly accepted by the family caregiver member that's present.

Now, one category of family caregivers that I think needs to be discussed in the future has to do with what happens if it's a mother who is

pregnant. Okay. And can we say or should we say that they might be excluded or they should be excluded with the understanding that if they're willing to accept the additional risk, it's the choice of the mother? In other words, it should be a should rather than a must type of scenario. But I think it's something that would require further discussion.

The process for allowing the 5 rem dose, I have allowable up there in quotation marks, requires again immediate notification of the following individuals or groups. Hospital management, the licensee's RSO. As I pointed out earlier, the NRC's regional office and if appropriate the agreement state agency. And the hospital risk management. These are individuals and groups that deal with risk scenarios involving workers, patients, visitors. Not just in terms of radiation events, but you know infectious diseases, other types of scenarios. And are well-versed individuals. And there is, at least in my investigation on this, is that every hospital has an individual who is designated as a risk manager. Now they may share other duties, but in larger hospitals especially in multi-modality hospitals, this is a sole designated individual that's involved in this. So it would reflect, I think, a non -- shall we say

radiation perspective of looking at risk to the family member, the caregiver as well as the institution in looking at various aspects of allowing a higher dose level.

In terms of the family caregiver, this individual would get a dose monitor. Now, this might be the only suggested additional expense that might be incurred by the licensee. Some licensees might have electronic dosimeters that are used. But what I'm seeing is that it would be something as simple as just maintaining an extra set of occupational dosimeters that are available for being assigned for this individual, which would be a relatively inexpensive means of providing these monitors.

The electronic types are somewhat expensive, involving several hundred dollars each, but you know leave it up to the licensee on how they want to accomplish that.

They will need to get radiation precautions and risk instruction as to what these radiation risks are involved. And it would involve as a documentation a radiation risk management, risk management consult with the risk manager.

Now, it was mentioned earlier that means of documenting this and providing this instruction

would be very timely or would be time consuming and be difficult to achieve. This is essentially is sort of a glorified informed consent process. Okay. Which is done on a daily basis, hundreds of times in a hospital. And I think it would be, again, a sort of a specialized means but it would be a means of providing this radiation risk information to the patient. It's a means of documentation. I think in this case the caregiver would get a copy of this, all right. And it would be done between the authorized user and the caregiver at a minimum.

So that all these processes of dose monitoring and the dose result, the precautions, the risk management consult, the informed consent would be all documentation that would be done and available for regulatory review.

So where do we go from here? Probably a suggestion is reviewing also NRC information on any previous events that are authorized to date. Dr. Zelac, and I think also in the NRC document before, there have been incidents evidently that either the region or headquarters have been involved with in authorizing levels above 500 millirems. It would be very interesting to see what was included in that process, what was documented, what was the

requirements of the licensee and use that maybe as a template to proceed as we go along. But not having privy to any of that information, it would be interesting to see what the differences are between what's proposed here and what has been done in the past.

I think guidelines with the NRC staff and the ACMUI will need to be drafted to address the various components proposed here and just simply as a means of trying to achieve a final result on this would suggest a final ACMUI review and approval of a proposed draft line by the fall meeting.

CHAIRMAN MALMUD: Thank you. Yes?

MR. ESSIG: I want to offer one problem. And that is we cannot allow dose limits to be exceeded without proper authorization. We cannot do that by guidance. It either has to be by rule or by exemption via license amendment. And unfortunately, I think that's a significant problem with what you've proposed.

There's a lot of good ideas there. Don't get me wrong. But I think to hinge it on a guidance document that we could issue; you mentioned a RIS and Reg. Guide, that sort of thing. We just cannot authorize licensees to exceed the 100 millirem dose

limit for members of the public with a guidance document.

MEMBER LIETO: Well, I appreciate that. I think you would even run into bigger problems just saying you want in regulatory space that you want to provide or allow members of the public to get some unnamed limit. I think you'd really run into some real difficulties with that.

If it does require it, it could be simply something as simple as your -- what is it -- the PSEs, the --

MR. ESSIG: Planned special exposures.

MEMBER LIETO: The special exposures. It could be someplace as simple as simple as that, just saying that this could be allowed and then it would -- and then in guidance that -- or the RIS mechanism would specify how you would implement that. But, I mean, if it has to a regulation as far as exceeding that, then fine.

MR. ESSIG: We had looked at the option of rulemaking. But then we also looked at the number of such cases that we would expected to see. And I think Dr. Sherbini pointed out that we only have the St. Joseph Mercy case and the one licensee in Pennsylvania that we had approved a priori exceeding the public

dose limit because of a series of children that were going to be treated and the necessity for the parents to provide care. And that case, it was 2 rem, as I mentioned was the limit that we authorized in the exemption.

And so that was the way that we have approached it. But the volume is so small that it wouldn't justify on a cost benefit basis undertaking a rulemaking because it would just -- that's what we have to look at. How many exemptions might we process? And if it's only a handful, literally, over a several year period, it wouldn't justify the cost of a rulemaking. That's the balance that we have to make.

MEMBER LIETO: From what I'm hearing is that to exceed this, to allow higher than this, requires rulemaking.

MR. ESSIG: No. But requires an exemption. Well, either a rulemaking that provides for a higher limit or an exemption to the existing regulation. And we can do that through a license amendment process.

MEMBER NAG: One of the thing is that because you have this rule, many people do not want to go through this exemption or ask the Commission and this kind of implant cannot be done on children. So if

it was an easy mechanism and it didn't require any special formalities, then more people would be willing to do implant in children. For example I know for sure I avoid low dose rate implant in children because of this reason. You know, this was -- although you are saying relative people have asked for an exemption, that too, but if it was available without meeting an exemption, more people may have attempted to do -- procedures.

MR. ESSIG: And I think as we noted, we're trying to work out the protocols of how this would be handled. I think they're very real problems of what Dr. Vetter mentioned, the 10:00 in the evening issue. Well, we don't have people on 24/7 duty to amend licenses. We fully realize that. But we do have an operations center and then we have a series of duty officers that are on call. I mean, that could at least constitute prior agency notice. They wouldn't get approval, but at least it would be notice.

And so some of the details are what we're trying to work out. But we would set up a process which would make for a more simplified and straightforward approval. That's the goal. And, Sami, correct me if I'm wrong, but I think that was the path you're heading.

DR. SHERBINI: Yes, that was basically what I was going to say.

There's just one other comment I want to make, and that is the 500 millirem limit, although it's true in Part 35, it's for patient release, there is a similar provision in Part 20 for members of the public that don't have to do with patient. So Part 20 does contain this provision. You can raise the dose to 500 without prior NRC notification or -- it's already in the regulations.

CHAIRMAN MALMUD: One thing seems clear, and that is that we're working toward a solution to what had been a problem in the instance in the hospital in Michigan. And that whatever mechanism we use must have either a rule or an exemption as part of the process.

DR. SHERBINI: Yes.

CHAIRMAN MALMUD: So Dr. Williamson?

MEMBER WILLIAMSON: Well, I think in the interests of having some mechanism in place soon, even though it may be the number of incidents is low, I think it's prudent to proceed with the development of a process for granting timely and rapidly license amendments. You know, I think the caution may be heard from several people, is they might to be really,

really more timely than your current administrative infrastructure allows for it to really be useful.

MR. ESSIG: We fully understand that, yes.

MEMBER WILLIAMSON: Yes. And I guess you can always look at the accumulated experience over a year and decide whether a rulemaking is warranted.

MR. ESSIG: Yes. Yes.

MEMBER WILLIAMSON: You're deluged by these amendments.

CHAIRMAN MALMUD: Dr. Suleiman?

MEMBER SULEIMAN: Yes. I understand your regulatory strategy, and I think I agree with it. But I think if you make the users aware of this amendment or exemption process ahead of time and lay out the guidelines or criteria, and I think, Ralph, you've laid it out real well, I professionally don't think that most any situation will exceed the 500 millirem. But it's nice to have that two-tier thing. It's going to force them to think. But I think if you allow them that option, I think you're going to be surprised. For the record, I predict that you'll get a lot more applications for exemptions than you think you would. And if that in fact plays out as you said, then it would be a justification for rulemaking.

MR. ESSIG: Yes.

CHAIRMAN MALMUD: Thank you.

If that completes the discussion of that topic, I wanted to think Mr. Lieto again and Dr. Sherbini for their presentations. And we'll move on to the next topic.

That would be Dr. Broseus. Oh, there you are. I hadn't seen you, that's why I hesitated.

DR. BROSEUS: Good afternoon.

Thank you for the opportunity to review where we're at with requirements for training and experience in Part 35. I'd just like to call to your attention that in your handout material and on the table we have provided copies of these slides, a copy of the *Federal Register* notice which includes the rule language for the revisions to Part 35, as well as a redline strikeout comparison between the effected sections in the final and the rule that was current before the publication of Part 35 amendments on the 30th of March.

The rule was published on March 30th and I've added to the material since you got your slides. The specific *Federal Register* citation was volume 30 of the *Federal Register* starting on page 16335.

This rule will be effective 30 days after publication; that is on April 29th of this year.

However, licensees will have until October 24, 2005 to implement the changes to the rule. This coincides with the extension of the effective date for Subpart J to October 24, 2005.

And lastly, agreement states will have three years to adopt the final rule.

The review I'm conducting today is not intended to be an extensive review of the changes to the requirements for training and experience in the final rule. Rather, I want to review the amendments with an eye to providing an overview of the nature of the changes to the requirements for T&E, and some of the major changes.

You may recall that the stage was set for this rulemaking by the Advisory Committee on the Medical Use of Isotopes, which I tend to lapse into ACMUI, excuse. It's an acronym I pronounced before I came to the NRC.

Okay. The ACMUI briefed the Commission on February 9, 2002 and called to the attention of the Commission a problem relating to the requirements for training and experience and the inability -- I shouldn't say the inability, but the fact that many boards would not be meeting the requirements. And so we'd be left in the pickle of not having board

certifications recognized, save for the one board which came in and met the requirements.

The NRC staff presented recommendations for rulemaking to the Commission in October of 2002 in SECY 02-0194. And this included attachment 2, not to this, but that SECY paper which was based largely on the recommendations of the ACMUI and its Subcommittee on Training and Experience.

Just going back over a little history for some members of the Committee who weren't here at the time, and for some members of the public might benefit from this, too.

Well, the final rule that we published in March reflects a culmination of ACMUI recommendation, a resolution of public comments on a proposed rule published in December 2003, as well as the extensive consultations between ACMUI and agreement states over the past three years. And these requirements in terms of key changes are changes to the requirements for recognition of specialty board certifications to serve as demonstrated adequacy of training and experience for use of radioactive material that is byproduct material, and also to sere as an RSO, an authorized nuclear pharmacist, authorized nuclear physicist. That combined with a preceptor statement which I'll

mention again in a moment, will get one approved to serve in those capacities.

As I have mentioned it applies for these four different categories. There are requirements that were in the rule that also apply to the so called alternate pathway, that is the pathway that's an alternate to board certification for administrating adequate of training and experience.

Preceptor statements were changed, highlights now, to use the word "attest" and "attestation" in place of "certify" and "certification." Now both the ACMUI and members of the public and agreement states felt that this would be a good change.

Preceptor statements are required for board and alternate pathways. However, the requirement for a preceptor statement has been decoupled from the requirements. Oh, that doesn't look good on a slide, does it? This thing. Hey. De-coopled. It doesn't look like that on my material. Anyway. Decoupled was a word that we used during some of the discussions. And the requirement for a preceptor statement still applies to individuals who are board certified, but it is not required for a board certification process to be recognized by the Commission.

Present in the original recommendations. Here's more manglement. Excuse the spacing here. It doesn't look like it's any place except on this particular computer.

In the original recommendations of the Advisory Committee and the attachment to SECY 02-194 there was a recommendation to add, I call it use-specific training for radiation safety officers and AMPs, and for a class of AUs in high risk uses. That is under section 600. This is gamma sterotactic radiosurgery and so on. So that requirement is also in the rule and applies to all applicants.

We're removed the requirement in section 390 for experience with elution and et cetera. Use of generators and so on. The ACMUI argued or mentioned one of our means we had over a year ago, I guess it was, that we felt that this training was not necessary for individuals to qualify under 300 and felt that the more general term experience and training and the preparation of dosage was adequate for this particular category.

We also decoupled in section 390 requirements for experience with oral and parenteral administrations from requirement for recognition of certifications. In this (b)(1)(ii)(G) of 390 there's

a requirement that individuals have experience with certain numbers of cases. That requirement is retained, but it is not required for a board certification to be recognized by the NRC or an agreement state. An individual would still have to demonstrate that they have this experience to be authorized for 300 use.

We added a new section 35.396, which is for the parenteral administration of unsealed byproduct material for which a written directive is required. This accommodates a group of physicians that was brought to the attention of the NRC by ACMUI and also recognized by some members of the staff. And that is a group of physicians that now qualify, for example, under Subpart J, but would not meet the requirements for section 300 uses. In particular, these are oncologists many times who have training and experience that's applicable to therapeutic use of unsealed material. The one addition the staff made here, the most important one I believe, is the requirement for 80 hours of training with unsealed sources. So that an individual who may have had experience with brachytherapy and be highly trained in radiation hazards and so on, we wanted to ensure that those individuals also had some training experience in

handling unsealed forms of radioactive material.

We have provided a pathway for medical physicists who are not named as AMPs to become radiation safety officers.

The final highlight I'd like to call to your attention is the petition resolves. Petition PRM 35-17. This is filed on behalf of the Organization of Agreement States. Most of us are familiar with this particular petition. The agreement states recommended that there be requirements established for minimum numbers of hours classroom or laboratory training for nuclear pharmacists in section 35, as well as for authorized users in sections 35.190, 290 and 390. These are basically uses of unsealed byproduct material, in 190 and 290, for which a written directive is not required and a 390 for which a written directive is required those being the higher risk uses. And that underlies the rationale for requiring a written directive.

I might note parenthetically that other sections do have requirements for minimum numbers of classroom and laboratory hours for high risk uses.

As many are aware, this is the resolution of what we came out of the discussions with. And I might mention again that as most of you are aware, we

had several conversations about this. And the most recent one I recall being with you all for the better part of four hours in a meeting not too long ago and which we discussed this at some length. And I want to come back to those discussions and the efforts that you have made in this regard in my concluding remarks.

However, let me note that for the various sections that we have listed on the table, there were already established in regulation space a requirement for total number of hours of training and experience that included classroom and laboratory training as well as other types of supervised training. But there was no requirement in these sections for a minimum number of classroom and laboratory hours. And the resolution and the rule is to require the numbers of hours for the various sections that we have listed here in the table. I want to note that this applies only to the alternate pathway and not to the board certification pathway.

And we also are now using the term "classroom and laboratory hours" rather than the "didactic" to make sure that it's clear what we're talking about.

And let me come back to the clarity issue in a minute reflecting on comments that Dr. Eggli made

this morning.

"Classroom and laboratory" seems to be a more acceptable term to many people for describing this type of training. And we are also using now consistently throughout the rule, I'm not using "didactic" in one section and "classroom and laboratory training" in another.

I'd like to take note, and this is not my slides, but react to some of the comments this morning from Dr. Eggli about the 200 hour requirement and in particular the suggestion that we should be more specific about what would be acceptable for that particular area. I will emphasize that the comments I'm going to make are somewhat spontaneous in that we haven't cleared this part of my talk with managers, but I want to emphasize what I'm drawing from is material in the *Federal Register* notice.

In our last big meeting on this issue the ACMUI actually talked about this issue before. And that is what is classroom and laboratory training. And in the *Federal Register* notice we take note that somebody -- and one of the stakeholders suggested that we define classroom and laboratory training. You might recall in the last meeting that there was considerable discussion about this and some people

said, "Well, be careful. You might get you ask for." And in fact, my personal view is that if you define the stuff too closely, you're becoming more perspective. And so one needs to -- when you go forward in looking at both sides of these issues, I would recommend that that particular part of the issue be kept in mind.

However, let me finally point out that we do have a discussion of this issue in the *Federal Register* notice talking about classroom and laboratory training. And I don't want you to go leafing through the fine print now, because I'll lose you. You can go look later on page 16350. I'm sorry 16349 under Issue 7, should the term laboratory training be defined.

And what we have said there is also reflected in draft revisions to our licensing guidance, in which we point out that the NRC feels that you have to take a broad view of what training is in terms of laboratory. There are structural educational programs, we took note in our discussions that there are other types of training programs that are more innovative. There's online training, etcetera.

Also we have included in the guidance that while the NRC expects that when credit is taken for

classroom and laboratory training for radiation safety that that's the area it truly should be in. But the NRC will broadly interpret training to include various types of instruction received by candidates for approval, including online training as long as the subject matter relates to radiation safety and handling of byproduct materials.

We also recognize in our discussion that some of this training may be in the clinical laboratory. And I'm using the terminology loosely, but the point is that we in the discussion in the *Federal Register* notice and reflected in our guidance, that it's broader. So I would suggest that those two points be kept in mind as we go forward.

After of the publication of the rule we move into the implementation phase.

Yes, sir?

MEMBER LIETO: Back on your last slide, how would those boxes be filled in in terms of total and classroom laboratory for the 396s, for 396?

DR. BROSEUS: 396, the requirement's for 80 hours of classroom and laboratory training. And for certification by a board recognized, as I recall, for 600 uses. Okay. That's one pathway. So if a person is certified by a board, recognized in 35.690 and has

it has 80 hours of training experience for unsealed sources, that's a pathway for --

MEMBER LIETO: Eighty hours.

DR. BROSEUS: Okay. Okay. Let's go on to the next phase.

When we publish a rule, we move into implementation space. And as I mentioned earlier in the slides, the licensees have until October 24th, 2005 to implement the final rule. During this implementation period, the NRC, the MSIB in fact, the Material Safety and Inspection Branch, has already sent out letters to boards inviting them to apply for a recognition of their certifications. We are in the final stages of revising licensing and guidance for medical use. This is NUREG 15.56 volume 9 revision 1, and we anticipate that being released to the public and published within the next couple of weeks, I should hope.

In parallel with that, there's a revision to NRC Form 313A. This is the medical use, training and experience and preceptor attestation form. This is the form that applicants may use to submit information about training and experience and preceptor attestation to the NRC to document the adequacy of their training and experience.

I didn't realize that you had moved on. Excuse me.

These will be available to everybody for implementation of guidance that I just mentioned, this will be available on paper. It will be mailed to licensees as well as being available on our website. This is under the medical uses licensee tool kit on NRC's webpage. And I've included the URL for your convenience here.

The *Federal Register* announcement which includes the revised language as well as the redline strikeout version, the highlights, changes, is available on the rule form and the URL for our rulemaking form is listed there.

I'd like to close with the following comment and then open up -- I think we still have a few minutes for questions, Dr. Malmud?

CHAIRMAN MALMUD: Yes. Yes.

DR. BROSEUS: With the publication of the final rule in T&E in the *Federal Register* on March 30th we collectively completed a complex multiyear effort to put into place regulations and requirements for training and experience of SROs, AMPs, ANPs and authorized users. The culmination of this effort is due in no small part to the work of the members of the

ACMUI, particularly the Subcommittee on Training and Experience. I offer my personal thanks for your efforts in this undertaking, especially and required to the modification requirements for recognition of especially board certifications to qualify individuals to serve as RSOs, authorized medical physicists, authorized nuclear pharmacists and authorized users. Thousands of licensees, NRC and agreement state staff, hundreds of individuals per year will benefit from these changes. This is on an annual basis there will be hundreds of individuals who will benefit from these efforts. So I am proud to h ave been a participant in this effort. And I am very thankful for the very considered thought and input of members of the stakeholder community, the public, agreement states and the ACMUI. Thank you.

Thank you.

CHAIRMAN MALMUD: Comments? Questions? Dr. Eggli?

MEMBER EGGLI: Thank you, Dr. Broseus.

However, let me say that I have to respectfully continue to emphasize concern that's emphasized by many members of the nuclear medicine community including an email that I have here from Dr. Berry Siegel, who most of you know very well. Being

a little perspective is like being a little pregnant. I don't understand the concept of "a little prescriptive." Once you're perspective, you're perspective. And training directors are going to have a lot of anxiety of what's going to qualify in the preceptor statement.

You know, didactic was an interesting definition. I could show you definitions of didactic, once you separate it to classroom and laboratory I am much more comfortable with the concept of classroom. But I am not comfortable with the concept of laboratory. Leaving it ill-defined allows in the regions some variable interpretation. And what may pass muster in one region may not pass muster in another region. And training directors are scared to death that they will write preceptor statements that will not be accepted for licensure.

Finally, 20 percent of diplomats of the American Board of Radiology do not pass their board examine first time. As a result, to work we will have to train all radiology residents who do over 70 percent of the clinical nuclear medicine in the United States to alternate pathway requirements. So to say that there is no prescriptive requirement for training for board certification pathway is technically true,

but functionally untrue. Because of that the fact that 20 percent do not pass first go around means that we are going to have to train all of our residents to alternate pathway guidelines.

The other question is we have a lot of people -- a follow-up question is we have a lot of people in the pipeline already. And now that we're prescribing specifically 200 hours and the preceptor statement, how are we going to get third year radiology residents who are actually fourth year post-graduate out of a five year training programs within that very short period of time up to October 2005 trained to the level where they can become authorized users? We have a very short time line for the people who are already deep in the pipeline with the fact that there was no previous prescriptive requirement for a board certification pathway. Now for my purposes as a person who has to design and operate these training programs, it is now prescriptive.

DR. BROSEUS: I really don't have an answer for your question because we're moving into an implementation phase of how the staff will look at people who are now in the pipeline. I would imagine that people who are certified by boards recognized by the NRC who meet the requirements, those people would

be approved.

MEMBER EGGLI: But they still have to have a preceptor statement?

DR. BROSEUS: Yes.

MEMBER EGGLI: And if that preceptor statement doesn't contain all of these elements, they may not get their authorized user status, even though they're board certified.

DR. BROSEUS: I don't know if anybody from MSIB is here wants to address that question. Anybody else?

CHAIRMAN MALMUD: I can't speak from that respect, but I can speak from the perspective of having heard -- I can't speak as a member of the board, but I can speak as someone who has received the same concerns that you have via the mail and email.

Number one, it is true as you point out that about 20 percent of the graduates of the training program will not be board certified for yet another year beyond their completion of their training, and therefore would have to meet the criteria set for those who have not yet passed the boards. So we'll accept that as a fact.

The changing of the wording from "didactic" to "laboratory to classroom" really gives

the training program director the kind of flexibility that he or she would need in certifying the trainee's experience in that even the minimalist approach to training in nuclear medicine will require three months of training in the course of the radiology residency. We're not addressing nuclear medicine residents, it is because they are a minimum of two years dedicated full time to nuclear medicine with all the time in the world to have accomplished these goals. But in radiology it could be as little as three months, which is 480 hours. Of that 480 hours, 200 would have to be "classroom and laboratory." The laboratory clearly now, as I have interpreted the messages that I'm hearing from those who have described it, including Dr. Broseus, includes the clinical laboratory experience meaning the experience in the hot lab and in the clinical lab. A clinical lab is, as we all know, what we do everyday. So I believe that we are covered.

The concern remains, and I'm expressing this not from my perspective but from the emails that I've received, that an overly zealous lower level employee in one of the regions may decide to redefine laboratory and clinical and say that the -- excuse me. Laboratory and classroom and may decide that his or

her career depends upon etching something in stone that wasn't there to begin with.

But it seems to me that with all of the documentation that we have of these discussions amongst ourselves and the presentations that have been made by members of the NRC staff including Dr. Broseus that there is a printed record of what the definition of -- how the definition of "didactic" has been changed to laboratory and clinical -- excuse me. Laboratory and classroom, and that we seem to agree that we shouldn't request any more definition because this will really meet the training -- this will mesh well with the existing training requirements and the number of hours spent in nuclear medicine.

Parenthetically, the number of hours spent in classroom by radiology residents includes relevant radiologic physics that applies to nuclear medicine as well. So some of the physics training that our residents get during the course of their four years of residency is certainly applicable to the radiation safety issues and to nuclear medicine physics.

So, in a sense we're better off the way it is it seems to me. I can't address what some over zealous employee may decide to do in the advancement of his or her interest or concerns. But it seems to

me that this distinguished group has defined that we meet the requirements.

MEMBER EGGLI: I disagree.

CHAIRMAN MALMUD: Doug?

MEMBER EGGLI: I have to respectfully say that I don't agree with your analysis and the definition of "clinical laboratory" is wide open for interpretation which could be interpreted in a wide variety of ways. And, again, as I am at risk in a couple of ways.

One is I could be -- our programs can be sued by candidates who now say that we have damaged them in the job market because we have inadequately prepared them because the preceptor statement we wrote didn't pass muster.

Again, I don't think you can have a partially prescriptive rule. I think if you say that the rule is we have to provide a body of knowledge and demonstrate mastery of body of knowledge in those skills, then it is up to me to define a training program. Once you start putting broad hourly limits on that requirement, you have made it prescriptive. And what you have done is made it prescriptive with uncertainty. And I think that is the worst of all possible situations.

CHAIRMAN MALMUD: And Dr. Eggli's concerns are the concerns that I have been receiving from other members of the radiology community who are very anxious about the subject.

Dr. Diamond, were you next?

MEMBER DIAMOND: I just wanted to point out the comment that Roger made on page 16349 of the *Federal Register* Issue #7, which is the first column on the left hand side, there is an extensive discussion regarding the definition and connotation of these terms, which I think would serve to the point that Leon spoke to a few moments ago as far as the discussion why it was opted not to become more prescriptive to provide more definitions and so forth.

So, again, in the hypothetical case of an over zealous regulator I think that this commentary should serve us very well.

CHAIRMAN MALMUD: Dr. Williamson? Oh, I think Williamson was next and then Dr. Nag, then Mr.--

MEMBER WILLIAMSON: Yes. I certainly have been listening to both sets of arguments of Dr. Malmud and also thinking about it from the perspective of radiation oncology, which will also be I think effected by the outcome of this. And I do have to say I think the statements of consideration, these

question and answers, really do set forth a body of material for the ultimate that would be used in an adversarial situation to try to resolve what is the meaning of the specific regulations. And I guess if the Commission has spoken, they may not in the near future be willing to reconsider rulemaking initiatives on this point again. And at least for the short term, you know, I think one should think very carefully about encouraging initiatives that would make it more prescriptive than it already is. Because that, as has been pointed out, might be more injurious and perhaps a certain amount of uncertainty is better than more clarification that restricts the practice of medicine even more.

So I should think a major practical initiative would be to try to get a reasonable set of residency guidelines approved via the American Board of Radiology, got that on the website, and that would go a long way towards encouraging the agreement states to accept a rational curriculum in radiology, and by extension in radiation oncology as well.

CHAIRMAN MALMUD: All right. Next is Dr. Nag.

MEMBER NAG: Yes. Dr. Eggli, you were concerned that 200 hours for nuclear medicine may be

difficult sometimes to meet for general radiology residents because of the short time is spent in nuclear medicine. But I am aware these 200 hours includes general radiology, radiation safety which is done in a general radiology residency. So some of that will overlap, wouldn't you think?

MEMBER EGGLI: There is a small amount of overlap. And I think we discussed this at our last meeting. At least in the didactic arena the overlap between what we consider -- and again, we've designed the classroom portion to be a reasonable curriculum. We have about a 33 percent overlap between radiology, physics and specific nuclear medicine physics. We spend a lot of time teaching specific physics of CT specific physics, of ultrasounds, specific physics of MRI none of which are directly applicable to nuclear medicine issues. We have about a 33 percent overlap in our curriculum between general diagnostic radiology physics and physics specific to nuclear medicine and radiation safety.

CHAIRMAN MALMUD: Thank you. I think Mr. Lieto and then Dr. Vetter.

MEMBER LIETO: Roger, the commentary that's in there that defines or clarifies the terms laboratory and classroom, are those going to be to

some extent in the NUREG document also? Because that's probably where the regions are going to be looking in terms of guidance. You know, if the very broad description of what that includes or addresses is there, I would think it might minimize over zealous interpreters, if you will.

DR. BROSEUS: Appendix D has a discussion. And there's a note that has been added that talks about classroom, laboratory, didactic training and the discussion that we just had. And it reflects the language rewritten for guidance. That's in the FRN.

While I have the microphone, I'd just like to build a little bit on the comments made by a couple of Committee members.

I believe personally from my experience as well as on one side -- on the other side as well as here that some creative thinking may be required but if one looks at the content required in radiation safety training, I think one in many cases will find more overlap than one might expect. There's training in radiation physics and instruments, radiation protection, radiobiology, chemistry of byproduct materials, radiation biology, radiation dosimetry and that's quite an expansive area.

I'd like to also note that when the staff

went through this they also had to take into consideration the concerns of the agreement states and the feeling that there needed to be a minimum established to be able to judge the adequacy of training programs. And so we have somewhat of a compromise here, but I believe that if this is tackled during the implementation phase, that it's doable.

I think that the issue that was brought up early about the people who were in this little window here, my own personal feeling is that the staff on the implementation side and the MSIB will look at these issues and try to work with them as much as possible. I can't speak officially for that group because I'm not a member of it, but my own personal experience in working with the -- see I'm on the rule writing group, okay, and there's an implementation group. And this group has been working very closely with people in the regions. They have monthly meetings to discuss issues and licensing issues. And I think there's room to work these out.

CHAIRMAN MALMUD: Thank you, Dr. Broseus.

We have several announcements to hear from Mr. Essig and then we have to be over at the Commission briefing. So is there anything? Excuse me, Dr. Van Decker?

MEMBER VAN DECKER: Can I just ask one quick question before Dr. Broseus leaves?

Now with the academic year ending in a couple of months do we see revised Form 313 coming out shortly or do we see ourselves still where we are for next several months?

DR. BROSEUS: The 313A?

MEMBER VAN DECKER: Yes.

DR. BROSEUS: Coming out shortly?

MEMBER VAN DECKER: Yes.

DR. BROSEUS: It should be available shortly on our website. We have a copy of it reproduced in Appendix B of the guidance document. But the form itself should be on the website by the effective date of the rule.

CHAIRMAN MALMUD: We have a member of the public who has been waiting. Can we hear that comment first? Please.

MS. FAIROBENT: Lynne Fairobent with AAPM.

Just two quick points. One, I'd like clarification of when the three years for the agreement states is effective? Is it April 2008 or is it October 2008? I've seen nothing in any of the documentation and clarifies. And from discussion I've heard it interpreted both ways.

And secondly, just a quick comment and concern about the reflection of the classroom and laboratory hours being discussed in guidance. Agreement states do not have to adopt the guidance. They only have to adopt the regulation. And I do think that there may be some concern.

I agree with Dr. Eggli's viewpoint that there may be some very different interpretations of what that is meant in the implementation phase in some of the agreement states.

CHAIRMAN MALMUD: Thank you for your comments.

DR. BROSEUS: Regarding the question about when agreement states have to implement, I can't answer that. I would have to defer it to ODC or Office of State and Travel Programs. I'm not sure what the date would work out to be.

CHAIRMAN MALMUD: Thank you.

Dr. Essig?

MR. ESSIG: Just quick announcements?

CHAIRMAN MALMUD: Please.

MR. ESSIG: We need to be over in our main building at 3:15 promptly. We actually need to be there before that because the Commission will actually start. It's the Commission Conference Room on the

first level. The tall building, Building One. If you walk past the guard, they'll direct you to where the Commission Conference Room is.

I would invite members of the public who are here to certainly attend that meeting.

Also remind members of the public that the Committee meeting tomorrow morning from 8:00 to 10:00 is closed to the public. So if you wish to participate tomorrow, come at 10:00.

CHAIRMAN MALMUD: Any other announcements?

MR. ESSIG: No.

CHAIRMAN MALMUD: All right. So we are adjourned to head over to the Commission meeting. Thank you.

MR. ESSIG: Yes. There is one other announcement for members of the Committee. That is for members of the Committee those presenters along with you will sit at the table opposite the Commission. The rest of the Committee will sit in a row down in what we call the well or the pit. You'll sit right behind the Committee members who are the table.

CHAIRMAN MALMUD: Mr. Essig reminds us that those who are presenting will be in the front row and everyone else in the amphitheater arrangement.

The pit. Thank you.

MR. ESSIG: The pit. Yes.

(Whereupon, the meeting was adjourned at 2:49 p.m.)