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NUCLEAR REGULATORY COMMISSION

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ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

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MEETING

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FRIDAY, SEPTEMBER 21, 2012

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The meeting was convened in room T-2B3 of Two White Flint North, 11545 Rockville Pike, Rockville, Maryland, at 8:00 a.m., Leon S. Malmud, M.D., ACMUI Chairman, presiding.

MEMBERS PRESENT:

LEON MALMUD, M.D., Chairman

BRUCE THOMADSEN, Ph.D., Vice Chairman

DARICE BAILEY, Agreement State Representative

MILTON GUIBERTEAU, M.D., Diagnostic Radiologist

SUSAN LANGHORST, Ph.D., Radiation Safety Officer

STEVE MATTMULLER, Nuclear Pharmacist

CHRISTOPHER PALESTRO, M.D., Nuclear Medicine Physician

JOHN SUH, M.D., Radiation Oncologist

ORHAN SULEIMAN, Ph.D., FDA Representative

WILLIAM VAN DECKER, M.D., Nuclear Cardiologist

MEMBERS PRESENT (Continued):

LAURA M. WEIL, Patients' Rights Advocate

JAMES WELSH, M.D., Radiation Oncologist

PAT ZANZONICO, Ph.D., Nuclear Medicine Physicist

NRC HEADQUARTERS STAFF PRESENT:

BRIAN McDERMOTT, Director, Division of Materials Safety and State Agreements

PAMELA HENDERSON, Deputy Director, Division of Materials Safety and State Agreements

CHRISTIAN EINBERG, Chief, Radioactive Materials Safety Branch

MICHAEL FULLER, Alternate Designated Federal Official, Team Leader, Medical Radiation Safety Team

ASHLEY COCKERHAM, Alternate Designated Federal Official, ACMUI Coordinator

SOPHIE HOLIDAY, Alternate ACMUI Coordinator

NEELAM BHALLA, FSME/DILR/RB-B

SUSAN CHIDAKEL, OGC/GCLR/RMR

JACKIE COOK (via webcast), RIV/DNMS/NMSB-B

DONALD A. COOL, Ph.D., FSME/DILR

SAID DAIBES, Ph.D., FSME/DMSSA/LISD/RMSB

SANDRA GABRIEL, Ph.D., FSME/DMSSA/LISD/RMSB

LATISCHA HANSON (via webcast), RIV/DNMS/NMSB-A

VINCENT HOLAHAN, FSME/DMSSA

ANTHONY HUFFERT, RES/DSA/RPB

ANDREA KOCK, OCM/WO

JEFF KOWALCZIK, FSME/DMSSA/LISD/RMSB

ANGELA MCINTOSH, FSME/DMSSA/LISD/RMSB

ANDREW PESSIN (via webcast), OGC/GCLR/RMR

JOSEPHINE PICCONE, Ph.D., FSME/DILR

LIZETTE ROLDAN (via webcast), RIV/DNMS/NMSB-B

DUANE WHITE (via webcast), FSME/DMSSA/LISD/RMSB

RONALD ZELAC, Ph.D., FSME/DMSSA/LISD/RMSB

PUBLIC PARTICIPANTS:

ROBERT DANSEREAU (via webcast), NYS Department of Health

WILLIAM DAVIDSON (via webcast), University of Pennsylvania

ROBERT GORSUCH, Johns Hopkins Hospital

KELLI HAYASHI, Johns Hopkins Hospital

KAREN LANGLEY (via webcast), University of Utah

RALPH LIETO (via webcast), Trinity Health

ANGEL MCCULLOUGH, Johns Hopkins University

JANETTE MERRILL, Society of Nuclear Medicine and Molecular Imaging

MICHAEL NOSKA, U.S. Food and Drug Administration

MICHAEL PETERS, American College of Radiology

DENNIS PHILLIPS (via webcast), U.S. Department of Energy

JOE RODGERS (via webcast), Theragenics

RUTH SCHUKMAN-DAKOTAS, University of Kansas Hospital

MICHAEL SHEETZ (via webcast), University of Pittsburgh

CINDY TOMLINSON (via webcast), American Society for Radiation Oncology

GARY E. WILLIAMS, VA NHPP

NANCY YOUNG (via webcast), Xcenda

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P R O C E E D I N G S

8:07 a.m.

CHAIRMAN MALMUD: The agenda today will begin with the presentation by Angela McIntosh entitled, "Abnormal Occurrence Criteria."

Angela.

MS. McINTOSH: Thank you, Dr. Malmud. Good morning. I am back here again to present on the abnormal occurrence criteria. And I've already presented on it a couple of times, as events develop you realize you have to come back, and it is best to get it right. So, I'm back here again and maybe this will be the last time I have to bring this before you.

But to give you a little background on -- to catch everyone back up to speed on how we got to where we are today, back in 2008 the staff identified that the definition of medical event -- the staff identified rather, that too many medical events were (audio interference) AO criteria.

What I mean by that statement is that we believe that too many relatively non-significant medical events were in the AO criteria and thereby --

(Phone interruption.)

MS. McINTOSH: And so, the staff presented some draft criteria at the 2008 meeting for the ACMUI to

discuss. And the ACMUI reviewed and discussed those criteria and recommended that (audio interference) the committee voted on it and the staff accepted that recommendation.

Well, in the meantime, the staff had to wait because per condition of the regulation, we could not open up the criteria and proceed with the change, because the Office of Nuclear Reactor Regulations portions of the criteria needed to - it needs to have a certain amount of experience with that criteria before they would entertain a change to the criteria. So, the staff had to wait.

And in the meantime while the staff was waiting, the committee changed some people and the staff also recognized that significant adverse effect might be a little too qualitative for the staff to use to make a determination whether a potential AO had occurred.

So, in December of 2011, the staff suggested that significant adverse effect be defined, because it was a little too qualitative.

The ACMUI again looked at criteria and what they did - I can bring it up - they recommended what you see on the screen right there before you. And basically, the ACMUI suggested that a designated consultant physician be employed to help determine whether an AO had

occurred.

Well, the management has been contemplating these particular criteria and has decided that these criteria as stated, the practical application of these criteria probably will be that we will have to hire a medical consultant in nearly every case that we come across a potential medical event - I mean a medical event, rather.

And that would, we foresee, would put an excessive burden on the AO determination process, it would slow the process down quite a bit, and present an excessive financial burden on NRC and the agreement states as the staff tires to make this determination.

Does this particular medical event that we're looking at - should we hire a consultant? Well, probably the default would be that we would have to hire one, because who would really be sure?

And so, criteria to screen the events seemed appropriate. Some criteria for staff to screen the events, to screen out events where we felt we probably wouldn't need to hire a consultant.

And so, the following slides will present an overview of some refinements that we have added to the criteria for your consideration. And subsequent to those slides we'll present some red line strikeouts of the

precise suggested refinements that we are presenting to you today. And the details of those refinements will be discussed.

So, here's an overview of what the refinements are. You will note that the title has been changed and footnoted on this slide. And there's some language added back to the criteria that looks significantly like existing AO criteria language.

On this slide, and you can't see on this slide, but we'll see it on another one, a phrase in bold font has been - well, actually you can't see the bold font part. "One or more" is the bold font, and the criteria are bulleted.

Now, this is where we discuss the changes in detail. The existing criteria says "For Medical Licensees," and we suggest that that be removed and replaced by "Events Involving Patients or Human Research Subjects."

We believe this has probably always been understood, but we thought it was important to make it clear that these criteria actually apply to patients and not to medical licensees.

There are other criteria in the AO criteria that apply to licensees. And so, we wanted to make it clear that these particular criteria do not.

Our second change there that you see on the bullet, "A medical event that results in," we've crossed out "death" and replaced that with "a dose other than the dose to the intended target."

Currently, the AO criteria do not specify that the target organ is excluded. And so, we've had instances where the target organ received a thousand rad above the prescription. And we've had to capture it as an AO.

And so, we didn't - that wasn't what we intended to do. So, this suggested change makes it clear that it's not the target organ that should be included in the determination, but some other organ or tissue.

And then the third edit that is presented as blue font on the screen, these criteria are substantially what we're using right now.

There's a minor change that we added. We reiterated on the third bullet that it's any other unintended organ other than the treatment site. It's reiterating what you see there on the - in the red line text above it, just to make it clear. And then there's an “and” statement.

So, these criteria in blue are functioning as screening criteria for the NRC staff. A medical event would have to at least meet these criteria before we would

even consider going forward to possibly determine that a medical consultant would need to be hired.

And then on this screen, remember there was an "and" statement before. So, one of those screening criteria would have to be met, and the event would have to result in a significant impact on patient health that would result in.

And then that language that the ACMUI recommended before, we've crossed that out and replaced that with "one or more of the following, as determined by a consultant physician deemed qualified by NRC or an Agreement State."

Then you have those four bulleted statements in front of you, unintended permanent functional damage to an organ, unintended permanent functional damage to a physiological system, a significant unexpected adverse health effect and death.

I want to point out a couple things about this suggested change. First of all, what the ACMUI already recommended is substantially there. It's essentially there.

If you look at the stricken out text, you will see "permanent functional damage." Well, that idea or that phrase is below in the red line text, "Unintended permanent function damage." It's there twice in two

different bullets.

And significant unexpected adverse health effect, which is part of the stricken out text has been carried forward. That's still there. And death as one of the criteria, is still there.

The reason why staff is recommending these changes that you see before you, is because we wanted to make it clear that only one of the criteria need be met, even though that probably was sufficiently evident in what the ACMUI recommended.

Still, this makes it very clear that only one of these criteria needs to be met, and not all of them, for an event to be considered a potential AO.

And then secondly, the staff suggests adding unintended permanent functional damage to a physiological system, because that criterion is consistent with other AO, with another criterion elsewhere in the AO criteria.

So, that whole idea with physiological system being unintendedly damaged, it just carries through the entire AO criteria whether you're speaking of the medical arena, or some other arena. And so, there's consistency there.

And then, another thing that staff did in bulletizing these criteria, was rank them. Because the

way the criteria had been presented before, the very first item on the list was "death", followed by these other things.

And so, the staff just believed that, you know, logically we would rank these criteria from relatively most severe - pardon me - relatively least severe to most severe in terms of consequence to the patient.

Footnote 17 Reference, this is where your handout will probably be most useful to you. Because with these slides, you know, you have to follow conventions about how big the text is and you can't put all this information on one slide and it might be hard to follow logically. So, if you refer to your handout, that will help explain Footnote 17 to you.

Remember that we suggest crossing out "For Medical Licensees" and replacing that phrase with "Events Involving Patients or Human Research Subjects" and footnoting that title.

And the footnote as you can see on your sheets there, says that criteria III.A.3 and III.A.4 also apply to medical licensees. And then immediately below the line there's criteria III.A.3 and III.A.4 presented before you.

And the reason the staff recommends that

this be explicitly stated in the AO criteria, is that this will be a way for the staff to capture what we believe should reasonably be considered an abnormal occurrence, but it is referring to the management of medical events, what could happen at a facility to cause a potential issue at that facility.

To give you an example of the kind of things that would be captured under these criteria, III.A.3 and III.A.4 in the medical area would be the VA Philly event in which the individual doses were not necessarily significant in the medical arena.

But the fact that so many repetitive errors occurred would be something that NRC would be interested in knowing about and something that we feel would be significant enough to report to Congress.

And so again, III.A.3 and III.A.4 are already in NRC's abnormal occurrence criteria. They're not new. But footnoting the medical arena criteria just makes it a little more clear that these criteria would apply at medical facilities.

Truthfully, we believe they would apply anyway. But again, this just makes it clear. Because if you read Roman numeral III there, it says "Events at Facilities Other than Nuclear Power Plants." Well, that would be a hospital. Just makes it more clear.

And so, to summarize the refinements that the staff is suggesting, we suggest that the current dose criteria be retained.

Again, NRC staff, we're not clinicians. And we can't make medical judgments. And so, it's helpful to us to have criteria to help us identify what we should look at a little bit more closely and screen out those things that probably do not need to be looked at more closely.

We believe that without these dose criteria, both the NRC and the Agreement States would probably need to hire a consultant for nearly every medical event that could possibly result in an unexpected adverse health effect.

We have clarified the criteria to make it absolutely clear that minimally only one set of - only one of the second set of criteria need to be met. We have ranked the criteria so that the significance are ranked from relatively lowest to highest. And we are proposing just to clarify in the criteria, that the generic trend criteria do apply to medical facilities.

Our next steps would be to obtain early Agreement State comment. We believe that this is important because the vast majority of licensees are in the Agreement States. And so, this would impact the

Agreement States significantly any changes made in this area.

After obtaining early Agreement State comments, we would send the criteria to the Commission for review. The Commission would include publication of it in the Federal Register for a 90-day comment period.

The staff would review those comments and incorporate them, represent the criteria to the Commission for a final review and approval. And then the final AO criteria would be published in the Federal Register.

And with that, I'd like to open up this item for discussion, Dr. Malmud.

CHAIRMAN MALMUD: First, Ms. McIntosh, I'd like to thank you for a very clear presentation with the historical footnotes for how it evolved. I think that it made it very easy for all of us to follow, because all of us had not been on the Committee over the term of these discussions.

And with that, I open the discussion for any comments from members of the Committee, please.

MEMBER WEIL: Just a clarification, please. This is only for events that do not involve the intended target. And I assume that the intended treatment target then is covered under the plus or minus 20 percent.

MS. McINTOSH: It would be a medical event to begin with to even be considered really to be an AO, but, yes. But exactly the event would have resulted in a differential of 20 percent in the dose. And so, yes, the target organ -

MEMBER WEIL: So, in a comprehensive definition of a medical event, should that not be reiterated, or is it unnecessary? I just put that out.

MS. McINTOSH: In a comprehensive -

MEMBER WEIL: This is a comprehensive definition of medical event, abnormal occurrence, right? That is what this is intended to be.

MS. McINTOSH: Yes.

MEMBER WEIL: But it only talks about doses to unintended organs outside the target.

MS. McINTOSH: Correct.

MEMBER WEIL: And I just wonder if it wouldn't be useful to include somewhere in there what constitutes a medical event that does involve the target organ. I'm just putting it out there.

MS. McINTOSH: I don't think I really understand your question. A medical event is - occurs when a prescription is made for a dose to an organ and that prescription is plus or minus 20 percent.

MEMBER WEIL: Uh-huh.

MS. McINTOSH: And that's covered under Part 35.

MEMBER WEIL: Okay.

MS. McINTOSH: So, when a medical event occurs and an additional, if you want to look at it that way, an additional error has occurred to the tune of unintended permanent functional damage or -

MEMBER WEIL: Any of these things.

MS. McINTOSH: - organ or system, that's an AO. It is a medical event to begin with. We wouldn't even look at anything that wasn't a medical event to begin with, because there would be no medical error.

MR. EINBERG: Angela, let me try asking if I understand Ms. Weil's question a little bit differently. Would there ever be a case where a medical event to the intended target would be an abnormal occurrence?

MS. McINTOSH: No, there wouldn't.

MR. EINBERG: Okay. So, then I think that's her question for discussion then.

MS. McINTOSH: No, there wouldn't. We are looking for something - I think I see what you're getting at.

If the target organ got so overdosed that permanent functional damage occurred, if that's what

you're saying -

MEMBER WEIL: Right, uh-huh.

MS. McINTOSH: - if that was not the intent of the prescription -

MEMBER WEIL: Exactly.

MS. McINTOSH: So, an example I can think of is a dose was prescribed to the thyroid. Maybe it was a diagnostic dose and the thyroid was ablated. All the dose went to the thyroid.

MEMBER WEIL: Or there was an error in the pharmacy or there was a misadministration.

MR. EINBERG: Angela, can you bring up the criteria?

MEMBER WEIL: It's your qualifying criteria that excludes anything that affects the target organ.

MS. McINTOSH: Target organ.

MR. EINBERG: Can you bring up Slide 6?

MS. McINTOSH: I think we want Five, actually.

MR. EINBERG: No, I was thinking about this one here, the proposed refinement.

MS. McINTOSH: Okay.

MR. EINBERG: If we were to take off "unintended" over the first two sub-bullets and just keep it as permanent functional damage to an organ or

permanent functional damage to a physiological system, would that address -

MEMBER WEIL: No, because it's the blue bullets. It's the blue bullets which have to be met first, before you proceed to the red bullets.

MS. McINTOSH: It's page - it would be Page 5. She's referring to the bullet that says "A medical event that results in a dose other than the dose to the intended target."

MEMBER WEIL: You're qualifying everything here to only involve things other than the target.

MS. McINTOSH: So, if the intended target got a dose, but that dose resulted - going back to the thyroid example, it was supposed to be a diagnostic, but it wound up being an ablative therapy, that would not have been intended, but the target, the dose did go to the target.

MEMBER WEIL: Uh-huh.

MS. HENDERSON: If we added in a dose other than the prescribed dose to the intended target, would that address your concern? Because then if it was more than what was prescribed, it could also result in an AO.

In other words, if the patient got two, three times what was - I see what you're saying that this would not address the dose to the intended organ. So, if the intended organ was overdosed, this language might

exclude that from being an AO.

MEMBER WEIL: Yeah, but that takes you back to where you were before where almost anything can be a medical event, because you're not putting in any thresholds there about what that target - what - the magnitude of the unintended dose, either under or overdosed, and you're back where you were before.

MS. McINTOSH: Because in that case and that specific example, it would be greater than a thousand rad.

MEMBER WEIL: Right.

MS. HENDERSON: Greater than or equal to a thousand rad to -

MS. McINTOSH: And then we repeat "unintended" there.

MS. HENDERSON: Right. So, we would have to add something a thousand rad greater than the intended dose and a thousand rad to any other unintended organ or tissue.

(Discussion off the record.)

MS. McINTOSH: A thousand rad greater than the intended dose.

CHAIRMAN MALMUD: Dr. Welsh.

MEMBER WELSH: I might suggest to address the important issue that Ms. Weil has just brought up that

maybe a medical event that results in a dose other than a dose to the intended dose to the intended target, and then to address Ms. Weil's concern. But then we also have concerns about these numbers, because they are organ system-dependent.

So, 10 gray for a thyroid is very different from 10 gray to the optic chiasm, or it could be very different from 10 gray to the spinal cord if given in a stereotactic fashion using a gamma knife, for example.

So, I'm not sure that these numbers are helping us, because they vary from system to system and technology to technology.

MS. McINTOSH: But these are only screening criteria though.

MEMBER WELSH: But there's an "and".

MS. McINTOSH: There's an "and", correct. That's where the real errors come in. The and, in this case, screening criteria to the significant things like unintended permanent functional damage.

CHAIRMAN MALMUD: Dr. Thomadsen.

VICE CHAIRMAN THOMADSEN: Addressing Ms. Weil's comment, isn't it caught by the term "medical events" in that bullet?

I mean, you're already triggering this because it's a medical event. So, do you need to change

the wording so that you pick up medical event again by referring to the target?

MEMBER WEIL: I don't know.

CHAIRMAN MALMUD: Dr. Suleiman.

MEMBER SULEIMAN: Yeah, I'm going down the same path. Medical event picks it up. Now, you're trying to determine severity. You're talking about some specific organs? You're assigning some different dose values.

I think once it's already triggered into a medical event, you really need a medical professional to assess it.

Dr. Welsh's point is you've got different technologies. I thought I made the point yesterday at least in terms of if you're dealing with unsealed sources versus sealed sources and external beam the precision and accuracy may vary. So, you've got uncertainty which organs are going to - in other words, I'd almost back off and say maybe use one number for all organs that would say, this is serious, this is a high number.

And then have somebody who understands whether it was a diagnostic procedure that wound up with a much higher dose, whether it was a therapeutic dose that wound up very, very wrong place.

This is a little confusing to me. And I think

maybe take a step back and come up to the more simple action limit with some experts analyzing what actually happened.

CHAIRMAN MALMUD: Dr. Thomadsen.

VICE CHAIRMAN THOMADSEN: Can I ask where the blue numbers came from?

MS. McINTOSH: This is what we currently use, actually.

VICE CHAIRMAN THOMADSEN: Where did they come from that you're currently using them?

MS. McINTOSH: Oh, where did they come - I would have to - I'm going to venture a guess. I'm not sure about this, but probably an NCRP or ICRP-recommended number.

CHAIRMAN MALMUD: Dr. Welsh.

MEMBER WELSH: I think the question at hand is do we need these numbers at all? Because I think they're leading to more confusion than benefit here. Because as we said, radiopharmaceutical therapy is so very different from gamma knife in terms of the effects of a specified dose that putting a specified dose, nominal figures in here, leads to more confusion than clarification.

CHAIRMAN MALMUD: Dr. Langhorst.

MEMBER LANGHORST: I like the criteria to

give to the staff to screen out medical events that don't need medical review.

I mean, it just - it helps minimize the number that they have to consider for adverse occurrence. And I understand that need.

I do think that Laura brought up a really good point. Because if you have an extreme dose to the target organ while this is a medical event, it's that results in a dose other than to the dose of the intended target. So, it rules out if you had a very substantial dose to the target that didn't result in any of these screening criteria. And that would not trigger that next medical review.

So, I understand the need to kind of sort out, okay, here's a medical event. Does it rise to the need to review for medical purposes whether it's an adverse occurrence?

But I'm not quite sure how to work in the target organ there like what you're recommending.

CHAIRMAN MALMUD: Dr. Thomadsen.

VICE CHAIRMAN THOMADSEN: Well, the question is to both - Dr. Langhorst first. I'm not sure we care if the target gets a huge dose if it doesn't have any physiological problems to the rest of the patient. I'm not sure that -

MEMBER LANGHORST: Right.

VICE CHAIRMAN THOMADSEN: Other than being a medical event, whether we need to worry about it being an abnormal occurrence.

To Dr. Welsh, I can understand why the staff would like a screening cutoff so that there's some de minimis error that they don't have to deal with.

Would it be possible to propose some cutoff level that could be uniformly applied that could both screen out the de minimis, yet be sufficient to catch both the optic chiasm case and any other case?

MEMBER WELSH: This is Jim Welsh.

I suppose the answer is yes that if we put in a lot of thought and effort, we would come up with numbers that would satisfy that criterion.

But I suppose the - my question is just because we've done this for so many years and staff likes it because it's comfortable, doesn't mean that we should continue to perpetuate this.

Because, you know, I guess we could come up with a number that would be good for spinal cord - cervical spinal cord gamma knife or optic chiasm, optic nerve and come up with numbers that would also be below - would be appropriate for radiopharmaceutical therapy or permanent implant brachytherapy, HDR brachytherapy,

et cetera.

But that exercise, in my opinion, is not very valuable, because we are going to be coming up with arbitrary numbers that I'm not sure I see the real value in.

And as long as we have that Boolean algebra there, that means that we don't - that we have to satisfy those numbers, that they are very important numbers.

And if we're struggling to come up with these numbers and some of us are questioning the real merit of these numbers, I'm not so sure that this whole category is worth keeping.

CHAIRMAN MALMUD: Dr. Langhorst, then Dr. Suleiman.

MEMBER LANGHORST: Dr. Welsh, do you feel that the numbers that are listed here would miss some adverse occurrences? Is that -

MEMBER WELSH: Absolutely.

MEMBER LANGHORST: - the point? Okay. And so, you're recommending that there be a medical review of all medical events? Is that -

MEMBER WELSH: Well, my point is that if you have a case of blindness that should not have happened, as an example, it would not fit this definition because of those numbers.

And if such a case could happen, then it illustrates that there is a deficiency in this proposed refined definition, as a quick example of why I feel like there is a deficiency.

CHAIRMAN MALMUD: Dr. Suleiman.

MEMBER SULEIMAN: Orhan Suleiman. I am also very concerned with the human research subject application, because - especially with radioactive drugs. You don't know. You're observing.

And so, sometimes patients get some - some of their organs get some pretty unpredictable, because that's the nature of research.

So, I don't know what that means to the research protocol, which is already under institutional review board oversight and IND oversight. So, are we - is it - is there double jeopardy here?

I mean, they have to - and during the research, they're obligated to report all sorts of observations. So, that would get picked up as part of the research phase.

MS. McIntosh: Okay. So, that for human research subjects there's a recognition. I think that what I'm hearing from you is that there is a recognition that something is unintended. But nevertheless, very severe if it happened.

And under the research protocols, that's accounted by whatever committees or rules that are under that apply to human research. So, you see it as redundant to -

MEMBER SULEIMAN: Well, when you subject a human subject to research, it involves protection not only from a safety point of view, from an ethical point of view. And so, the purpose of the research is to document everything you see.

Some of it's not very serious, but document everything because, you know, later on some minor side effect may turn up when you expand the study size or maybe it goes - the drug gets approved and you start using it on hundreds of thousands of people.

All of a sudden you say, oh, we may have seen this earlier, but now it's much more serious. But that's more of a non-radiation effect, but the objective is to follow all those.

MS. McIntosh: But does it make sense for NRC to have a licensee that does this and something goes awry and is significant and we know that it happened under an NRC license and we don't report it to Congress?

MEMBER SULEIMAN: Yeah, I don't know. I mean, I'm saying we should be picking it up assuming the researcher is doing what they're supposed to. I mean,

there's always that caveat, but we should be picking it up.

But if it's related to the product that you regulate, if it's related to the radioactive source in some way, form or another, maybe you need to be aware of it, you know.

CHAIRMAN MALMUD: Dr. Langhorst.

MEMBER LANGHORST: But Part 35 covers human research subjects in medical events. I mean, they're already in there. So, I don't think - if they're not doing the administration in accordance with their own procedures and they're plus or minus 20 percent whether it's human subject or patient, I think it's still under NRC purview and it makes sense to be included in here.

MEMBER SULEIMAN: You're regulated. So, that's fine with me.

(Laughter.)

MEMBER LANGHORST: I'm not saying I like it.

MEMBER SULEIMAN: If it works, you know, if it's working, that's fine.

CHAIRMAN MALMUD: This is Malmud. Raising Dr. Welsh's point, are we trying to achieve something with uniformity that's really not applicable to the use of radiopharmaceuticals versus the use of external radiation from a sealed source, versus implants? Are we

trying to develop a single code for all when it is not applicable?

And with respect to Dr. Suleiman's comment, is any of us aware of a permanent damage from a research radiopharmaceutical that was - that occurred as a result of the radiation rather than the pharmaceutical implant?

Is there any awareness of such an episode in the past? I'm not aware of any. There are radiopharmaceuticals which have caused difficulties because of the pharmaceutical employed which had untoward effects, but I'm not aware that the radiation burden was an issue.

Has there ever been such an example?

MEMBER SULEIMAN: Oh, I think that there were therapy trials where, I mean, these are trials. These are investigational drugs where patients get some pretty serious doses.

CHAIRMAN MALMUD: Radiation -

MEMBER SULEIMAN: From the radiation.

CHAIRMAN MALMUD: From the radiation? In diagnostics, or just therapeutics?

MEMBER SULEIMAN: These are oncology trials.

CHAIRMAN MALMUD: These are therapeutics?

MEMBER SULEIMAN: Yes.

CHAIRMAN MALMUD: Dr. Thomadsen.

VICE CHAIRMAN THOMADSEN: I don't have the reference. I think there was a Swedish trial quite some time ago using strontium-90 for metastatic prostate bone pain where the radiation did cause severe injury.

CHAIRMAN MALMUD: Again, that's therapeutic.

VICE CHAIRMAN THOMADSEN: That is therapeutic, yes.

CHAIRMAN MALMUD: I've only been involved in the field for 40 some years, but I don't recall a diagnostic radiopharmaceutical having untoward radiation effects from the radiation associated with the pharmaceutical, only from the pharmaceutical that was in trial.

Once again I raise the question, are we trying to do something that really is not achievable in applying the same criteria for diagnostics, therapeutics, in radiopharmaceuticals and for external beam radiation and for sealed sources such as implants?

Dr. Welsh.

MEMBER WELSH: To respond immediately to your question, I think that we are trying to do something which is not impossible. As Dr Thomadsen pointed out, we could come up with some numbers. But as I pointed out, it's a difficult exercise and I question its value.

But to solve this, I'm just wondering about that Boolean algebra and substituting it with an "or" would satisfy NRC's desire to have some numbers.

But by not making that an "and," it would minimize the relative importance of those numbers, which would be very difficult to come up with something that satisfies teletherapy, HDR, et cetera, et cetera.

MS. McINTOSH: Dr. Welsh, that would put us back to where we are currently, though. Which anything greater than a thousand rad, I mean, every permanent implant brachytherapy that was just off by a little bit would be an AO the way it is right now. Then an AO report has - we have a total of 15 AOs, and 12 of them are medical.

MEMBER WELSH: Then I would recommend getting rid of this entire section of nominal figures then. I think it's just not as valuable as we might think it was in the past. And it's too difficult to apply when we're trying to come up with numbers for radiopharmaceutical therapies versus gamma knife, versus HDR, versus permanent implant brachytherapy.

The numbers would be very difficult to come up with that would make sense.

CHAIRMAN MALMUD: Mr. Einberg.

MR. EINBERG: Just to reiterate, our goal here is to have the screening criteria so that the AO

criteria is practical or implementable.

And if we don't have some kind of screening criteria, then it puts the staff and the Agreement States in a position where they have to get a medical consultant or a physician to screen every medical event across the country.

And it's not implementable unless we have some kind of de minimis threshold for us to make that cut and say if it meets this, whatever the criteria is, then go ahead and get a medical consultant.

I think if we go forward without any screening criteria, the Agreement States will probably - or we've already, you know, we're hearing that, you know, in this tight budgetary time frame, you know, to get a medical consultant is, you know, very costly and is it really necessary to have a medical consultant for things that most likely are not significant anyway.

CHAIRMAN MALMUD: Well -

MEMBER WEIL: The purpose of a good screening tool is to be overly sensitive. And if I'm hearing Dr. Welsh's concern, there will be events that will not be picked up using these criteria. So, it's not sensitive enough; is that fair?

MEMBER WELSH: Yes.

MEMBER SULEIMAN: I think I'm speaking - I

think this is confusing to me, and I get a sense it's confusing to other people, but I'm going to take a step back.

And if you want to segregate these into brachytherapy, external beam, unsealed sources or radiopharmaceuticals and try to apply some criteria to each of those, would it make more sense and be less confusing?

I mean, I think part of the problem is we're trying to set numerical standards for very different sources that behave very differently in the body and for which the uncertainty in estimating those doses either to the organs or the body vary greatly.

But if you were to segregate into these three categories, would it make more sense if you came up with three different sets of numbers?

What's going to happen here, you're going to have a bunch of people look and say, what's that mean? How do we evaluate this?

And so, you're going to have, you know, you may bring in people who understand the language, but don't understand the underlying science.

MR. EINBERG: That certainly is an approach and, you know, would be implementable. But, you know, what are those numbers, I guess it comes down to.

MEMBER SULEIMAN: Well, I think I could come up with some numbers off the top of my head, but I won't use them - try it now if you were to segregate them by those sources, but I'm still trying to cope with these numbers that you have there.

CHAIRMAN MALMUD: Dr. Zanzonico.

MEMBER ZANZONICO: Pat Zanzonico.

I guess the question I have is do the screening criteria need to be part of the formal definition of an abnormal occurrence?

In other words, couldn't the - because what I'm thinking is you have this and so that in order for an event to be formally characterized as an abnormal occurrence, it would have to meet these dose criteria, as well as the subsequent clinical criteria.

The sense I'm getting is that it's really the clinical criteria that matters. So, couldn't the screening criteria be separated from the formal definition of the medical event and used administratively, for lack of a better term, by the NRC staff to pursue it? And since they would then not be part of the definition if you had an occurrence like the one Dr. Welsh described where there was an inadvertent dose to a particular radiosensitive part of the body that had a significant clinical sequelae, that would be captured

as an abnormal occurrence?

MR. EINBERG: I would say that, yeah, that's a possibility if the screening criteria are clear enough for a non-physician or, you know, to make that determination.

CHAIRMAN MALMUD: Dr. Thomadsen.

VICE CHAIRMAN THOMADSEN: It sounds like you would then be in the position though that you would for each medical event, you'd have to hire a consultant to evaluate whether there was actually permanent functional damage to an organ or a system.

MEMBER ZANZONICO: Well -

VICE CHAIRMAN THOMADSEN: Or maybe death if you need a consultant to establish that.

MEMBER ZANZONICO: Well, again, Pat Zanzonico. Just getting back to the example Dr. Welsh raised if, say, the dose criteria were not satisfied in that instance, yet there was an overdose - an avoidable overdose to the optic nerve or optic chiasm and that subsequently was recognized that the patient became blind in that - in the affected eye, then at that point it could trigger a review.

It would seem that we have a cause and effect relationship that would be recognized subsequently between the irradiation and the clinical effect even

though these particular dose criteria were not reached.

So, in that case, yes, you would need a medical consultant, but that would be a very obvious effect. But I still think you need, I mean, I sympathize with the NRC staff. You need some objective criteria so that you don't need to hire a medical consultant in every instance.

MS. McINTOSH: I would just add, Dr. Zanzonico, that the screening criteria wouldn't make it an AO. The screening criteria would be just that. It would just be a starting point for NRC to look - it's not that the screening criteria and these other criteria together make it an AO. It's just that the screening criteria is used to segregate out those that could meet these other criteria.

MEMBER ZANZONICO: But there is an "and".

MS. McINTOSH: There is an "and".

MEMBER ZANZONICO: So, it would have to be both. So, I think Dr. Welsh's point is there were instances where there are abnormal occurrences where the dose criteria would not be met, yet there would be a clinically significant effect. And that would not be an AO according to the way this is written, because there's an "and" in there.

CHAIRMAN MALMUD: Dr. Langhorst, then Mr.

Einberg.

MEMBER LANGHORST: Let me suggest this, because I think it may get back to Laura's point about the target organ and so on. And that's the criteria III.A.3, a serious safety-significant deficiency in management or procedural controls.

And that might be the catchall that NRC staff could use that if the target organ got way too much dose, that would be something that that safety-significant deficiency, you'd have to have a physician review of that for the patient and it would catch perhaps those criteria that maybe it doesn't obviously meet the criteria of the dose that you're using for screening.

I offer that up that that might be your catchall there. And I don't know if you mean that to be to apply to patients and human research subjects, or to other aspects of the program, of the radiation safety program for medical use licensee.

CHAIRMAN MALMUD: Mr. Einberg.

MR. EINBERG: To respond to Dr. Langhorst's question, I'm not clear - I'm not sure I understand how that would apply in -

MEMBER WEIL: It's too subjective.

MR. EINBERG: It's too subjective, as Ms.

Weil said. So, the practicality of it for us would still kind of get us into the position where we would have to get a medical physician or consultant.

MEMBER LANGHORST: Right. I mean, you have to have that in order to make that determination for III, don't you, a safety-significant deficiency?

MEMBER WEIL: No.

MEMBER LANGHORST: If it applies to a patient or a human research subject, you certainly would want medical -

MS. McINTOSH: That is meant to apply to the facility management.

MR. EINBERG: These are for events at facilities. And this is -

MEMBER LANGHORST: Nothing to do with the -

MR. EINBERG: With the patients, yes.

MEMBER LANGHORST: Then you need to get rid of the criteria.

(Laughter.)

MEMBER LANGHORST: Because you don't, I mean, you need a catchall someplace here.

CHAIRMAN MALMUD: The discussion has raised two important points. One by Ms. Weil, which is that she reminds us that the screening procedure is a screening procedure and it should be sensitive.

Then Dr. Welsh's comment that even with these criteria, it's possible for there to be a catastrophic event in radiation oncology not covered by these screening criteria.

So, it seems to me that we have not achieved the goal, because both of those comments are valid.

I also keep looking at this and say we're trying - it's as if the space program and commercial aircraft are to be governed by the same rules. They're not the same thing. They both go up in the air, but they're not the same thing.

And these are all radiation-related issues, but they are not the same thing. And, therefore, should we - these criteria that have been presented to us, from my perspective, are applicable to diagnostic radiopharmaceuticals, clearly.

I can't speak to their applicability to radiation oncology, but Dr. Welsh has spoken to them, and they're not - they don't achieve the goal there.

And I'm not even certain that they would have fit the issue that raised the concern at the Philadelphia VA so that I think we need to look at this with two separate sets of rules.

The staff out in the field needs criteria, we all agree, that can't be too subjective. We can give

them objective criteria if they were suited to the particular applications. Not individual applications, but the particular specialties of nuclear medicine diagnostic, nuclear medicine therapeutic and the various fields of radiation oncology so that there would be, I think, the need to look at these as separate issues.

Now, what about the issue of diagnostic radiology, for example, in cardiac - well, in issues where the cardiologist or the radiologist exposes the patient to an excessive amount of radiation during the course of the procedure?

Is that governed by this as well, or is that a separate issue?

MEMBER VAN DECKER: You're asking about machine producing radiation, Doctor?

CHAIRMAN MALMUD: Beg your pardon?

MEMBER VAN DECKER: You're inquiring to machine-produced radiation?

CHAIRMAN MALMUD: Yes, machine. That's radiopharmaceuticals.

FEMALE PARTICIPANT: That apply in an Agreement State.

MR. EINBERG: Just to go on the record, they would not apply and we do not regulate that.

CHAIRMAN MALMUD: So, then we have a simpler

issue. We simply have the nuclear medicine approaches and the radiation oncology approaches. I just wanted to clarify that.

Dr. Suleiman.

MEMBER SULEIMAN: Orhan Suleiman.

FDA has had reported incidents of serious overdoses from CT, from fluoroscopy. So, those things do happen from diagnostic procedures.

CHAIRMAN MALMUD: Are they dealt with by the FDA?

MEMBER SULEIMAN: Yes.

MR. EINBERG: And the FDA has their own criteria, which is -

MEMBER SULEIMAN: Serious adverse event, serious adverse event. Let me add earlier there was an incident a number of years ago and I know it was public, and I forget the - it was an isotope. It was used for research. And instead of the - I think the critical organ was supposed to be the kidneys or it was the other - or the bladder.

Anyway, they wound up giving a lethal dose to the kidneys and they didn't find this out until, you know, six to 12 months later. So, that's an example where the wrong organ got the dose for a number of reasons. And there was a lot of publicity and publications out of it.

To be honest, I wonder if that ever got reported as a medical event to the NRC. It was under trials.

CHAIRMAN MALMUD: It was an FDA issue.

MEMBER SULEIMAN: Oh, definitely, but it was a radioactive -

CHAIRMAN MALMUD: The last thing the country needs is duplicative regulations. If it's handled by one agency, it needn't be handled by the other as long as one agency or another is dealing with it. That's just a personal comment.

However, I still remain concerned about the points that Ms. Weil made and the point that Dr. Welsh made. And that is that these screening criteria will not apply to certain situations in radiation oncology that might result in untoward effects. And, therefore, I think we need to revisit it.

The criteria that you've presented, I believe, are perfectly applicable to diagnostic nuclear medicine procedures.

MS. McINTOSH: So, then, do you believe it would be prudent then for the Committee to come up with a screening criteria for therapy and we just - we keep these for diagnostics?

CHAIRMAN MALMUD: I would want to hear the

Committee's opinion about keeping these. I personally see nothing objectionable then and I see everything applicable in them, but that's just one man's view on nuclear medicine as it relates to this.

With respect to radiation oncology, we may need a radiation oncology subcommittee to deal with this and come up with criteria that are applicable to radiation oncology.

If then the people in the field have one set of guidelines for nuclear medicine and one set of guidelines for radiation oncology, we would have met our responsibility in giving them guidelines that will assist in patient safety and not interfere with the practice of medicine in both disciplines.

Dr. Welsh.

MEMBER WELSH: There's been a lot of valuable discussion and important points raised. And I might offer a suggestion just to throw down as a practical solution to see if this would solve the concerns that have been raised.

Number one, Ms. Weil has brought up the question of excluding the target. So, how about if we change the wording to include a dose other than the intended dose to the intended target.

That would allow us to include erroneous

doses to the intended target rather than exclude the target entirely.

The second point was my concern about these nominal figures, which I still think they're held over from an era that is long gone and not necessary, but I appreciate and I'm sensitive to those who like these.

Therefore, I might suggest like Dr. Thomadsen said, come up with some numbers that are more appropriate and that would be much lower and capture everything that could be in this abnormal occurrence, including lower doses to the optic chiasm, lower doses to the gonads if we're talking about fractionated teletherapy, et cetera.

And then finally on the next slide where we have the two bullet points unintended permanent functional damage to an organ or physiological system, I might suggest adding the word "unexpected." So, unintended and unexpected permanent functional damage.

Because unintended of course, but unexpected means that - it means something different. Because we know that radiobiologically there are thresholds that make possible unintended effects unlikely to have been related to the radiation itself depending on the clinical circumstances.

Radiation sensitivity, hypertension,

diabetes, these predispose individuals to more likely consequences of doses of radiation, as an example, that might be unexpected. Certainly they would be unintended, but would they be expected?

So, those are just some - a first attempt at a practical solution to the problem at hand.

CHAIRMAN MALMUD: Thank you. Dr. Guiberteau.

MEMBER GUIBERTEAU: Yes, I agree with most of what Jim said and I think the sentiment that's going around here.

I would really not like to see the screening criteria go away, because I've had a concern for a long time that this really roots this in what we're supposed to be doing. And that is radiation - the medical effects - adverse medical effects of radiation and I think these are very helpful.

I do agree that they're not as sensitive as they need to be. If we get rid of them, then there is, you know, reporting these things is not necessarily benign to those physicians who are treating patients who fall accidentally, because there are effects that are not covered in here that are not just unintended, but they're unrelated or incidental. And I think the screening criteria are a way of, you know, are a way of getting around that.

I agree very strongly that from a, you know, whether you're talking about - and I know that it's not covered, but diagnostic radiology and radiation oncology or nuclear medicine that I think trying to get one set that fits all will either make it too sensitive for some areas, and not enough for others and I would really encourage the ACMUI to ask for criteria that fit what we do, the major categories.

And I think like Dr. Malmud, I think that makes sense to me. And I think that would solve several problems.

CHAIRMAN MALMUD: Dr. Suh.

MEMBER SUH: So, I think this is a complex topic. And I think the two issues we have are we need the screening test that's sensitive. But at the same time, I agree with the sentiment around the table where that we also need a specific modality.

So, as Dr. Welsh pointed out, this criteria are greater than or equal to 10 gray, that means very different things to the optic chiasm versus the spinal cord.

And I could think of a scenario where someone, lets say, has gamma neck radiosurgery the optic chiasm gets nine gray. Which in some people's estimation is a pretty high dose particularly if it's unintended and

it caused blindness to the patient.

With this criteria, you know, question is would it be caught or not. So, I think it does need to be specific to modality. Because if you're talking about brachytherapy, the dose of 10 gray over a couple of months is very different than giving it in one single session like in gamma neck radiosurgery. So, I agree that I think it needs to be specific to modality.

I think these are very generic numbers and I think there's a chance that you're going to miss some abnormal occurrences which should be reported.

CHAIRMAN MALMUD: Thank you. Dr. Van Decker.

MEMBER VAN DECKER: Just a couple of comments, if I may. I guess one reminder to all of this is that every case that's going to fit into this category almost by definition had to have fit medical events, right?

So, all of these are being looked at. There's a root cause being done on all of these for systems errors and everything else. So, there is a screen.

The screen is did you make medical event? So, that's our screen and we have a universe out there and we have people looking at it at the State level and people looking at it at the NRC level.

Now, we're talking about a second screen. A second screen that would raise it to the level of, you know, would it be reported at the Congressional level, would we be taking a higher resource to look into this?

So, then the question is, where is that second screen before we get everybody, you know, running in a circle?

And in Orhan's point, I think this is similar in clinical trial work when we talk about adverse events versus serious adverse events where we raise that second screen.

And I think as you would well point out, these red bullets here, the unintended and unexpected stuff is actually very similar to the wording that goes into serious adverse events.

Now, obvious in clinical trials irrespective of the radiation piece of it, which is an extra piece of this to the screen, you know, I can see many pragmatic reasons for why staff would like a number cutoff to say, well, that's clearly in a medical event, this just could be looked at, at medical - at root cause they are in, you know, we may not need to be looking for high enough that we definitely need a medical expert to say, well, put it back into the medical event category and root analysis there versus, yes, I think this is the

highest level of abnormal occurrence and it stays there rather than going back into the other medical event area.

What that number is, I think you can have lots of different views on it. And I think that's going to be the problem here trying to come to some consensus, you know.

The last comment I want to make because I don't want to get lost in all of this is where this Paragraph Number 3 fits in, because this is making me really confused here.

You know, I think as our State representative pointed out, both III.A.3 and III.A.4 are fairly subjective in nature to some degree. And, you know, if you put them in as an or situation as I think was proposed irrespective of the top two pieces, then you bring up the question of who's making the decision process on, you know, what is significant deficiency and what was a procedural control or generic, you know, I think that that kind of fits into the category.

And I think we had this conversation on the teleconference call about this topic is that I think that the real or at the bottom is, or under the discretion of the staff and the agency. Which means it didn't fit any of these and that's okay, but we think we wanted to report it to do some due diligence here.

But I think once you start getting into, you know, subjective kind of things and the question becomes, what's the adjudicating body for Three and Four, is that a physician, is that a systems management person and how do you really sort out that piece of the puzzle, you know, those actually look more fuzzier to me than some of the stuff we're talking about up above, actually.

So, I can see that point, but I'm not quite sure how it plays in.

MS. McINTOSH: I would just like to remind the Committee that we believe we've already actually seen an example of III.A.3 or Four. And that would be the VA Philly events.

If these new criteria were in place, they wouldn't have captured the VA Philly events. But the fact that there were numerous events is - makes it obvious that there was some sort of programmatic breakdown.

And that's what this, you know, trending for generic implications probably will not be that complicated.

MR. EINBERG: And just - I'm sorry. And just to add, you know, we have inspectors. The inspectors go out and inspected the VA. And whenever there is a significant event like this, then, you know, they bring their results back and it gets a lot of discussion and

management review here.

And if there is a determination made by NRC staff that there has been significant program breakdown, that's incumbent upon us to make that determination and report to Congress.

MEMBER VAN DECKER: Discretion.

MR. EINBERG: Absolutely.

MEMBER VAN DECKER: But at the same time if we looked at the top piece of this, we would say anything that fits into this category. Whether we've put in a radiation number, plus the clinical stuff, or clinical stuff alone, the root cause of that is either going to be human error or systems error or, you know.

So, it fits into the category. I mean, you have to have a breakdown of where you came from. So, I mean, this explains some of that other piece of it.

I'm not sure it adds other than, you know, common sense root cause analysis stuff, but that's fine because I understand the last piece is discretion. I got that.

CHAIRMAN MALMUD: Dr. Thomadsen.

VICE CHAIRMAN THOMADSEN: I had some comments on that. But, first, if you go back to Slide 5, please, by inserting the green intended on the dose, that would eliminate those medical events so as the target receives

the correct dose, but other organs do not.

Such as if the prostate were to have gotten its correct dose, but at the same time the rectum received a dose higher than 150 percent of what was intended, the dose other than the intended dose to the intended target would not be triggered.

So, this whole thing would not - it could never be an abnormal event. So, I don't think we want the green test there.

And going back to III.A.3, I agree with Dr. Van Decker here that how this would be used is a definite problem.

Back in the days when there was the QMP rule and we had a misadministration with no other violations, we were cited as violating the QMP only because the - if we had a misadministration, we therefore could not have had a QMP that would have prevented the misadministration. So, we were in violation.

And one could say if you had an abnormal event, therefore you obviously fail in III.A.3 where you could not possibly have had an abnormal event.

CHAIRMAN MALMUD: I have a question. I thought that III.A.3 applies to situations that don't necessarily involve patients at all. For example, having a one curie technetium generator in a room which is

unlocked. That would be a III.A.3, wouldn't it? A serious safety-significant deficiency in management -

(Simultaneous speaking.)

CHAIRMAN MALMUD: Beg your pardon?

MS. McINTOSH: No, I don't believe so.

CHAIRMAN MALMUD: That wouldn't be covered by this?

MS. McINTOSH: We have a process called the agency action review meeting in which we look at procedural issues at licensees facilities. Because even though an individual event may not be significant, the fact that there is a procedural issue, a repetitive problem which could lead to a bigger issue is something that the Agency has always been concerned about, has always looked at.

So, it's not necessarily that a significant error occurred. It's a precursor kind of - it's the identification of a precursor to a possible significant error. That's all this is looking at. It wouldn't - again, going back to the - I keep using this example, but back to the VA Philly example. I think most people would agree that the individual cases there were not significant relative to, you know, a very serious event at a medical facility.

But the fact that there was one incident

involving one specific physician, an incident involving a specific physician which so many patients got the wrong dose, is something that NRC would be interested in, is something that we do believe Congress will be interested in.

They would be interested to know that at Hospital X in the year, you know, 2008 there were, you know, 118 errors in this one procedure.

We believe that they would be interested in knowing that. And that's all this kind - that's all these criteria are intended to capture. It's programmatic generic - programmatic things with generic information.

CHAIRMAN MALMUD: There already is a system to capture the department that has a moly generator for technetium production with a curie in it in a room with no safety controls on the door so that anybody could walk in.

Reading this, it seems to me that that is included here. May be included elsewhere, but it's also inclusive here.

Isn't that a serious safety-significant deficiency in management or control?

MS. McINTOSH: I don't believe that one incident of deficiency in management or procedural control would be what we would capture to report to

Congress necessarily.

MR. EINBERG: But it possibly could though.

CHAIRMAN MALMUD: It possibly could.

MR. EINBERG: Yeah.

CHAIRMAN MALMUD: Homeland Security would be interested to have a curie sitting around unprotected. All right. Just a question.

Dr. Thomadsen.

VICE CHAIRMAN THOMADSEN: Just a question also in the title on Three, are those events at facilities other than nuclear power plants and other than all transportation events, or is it other than nuclear power plants and now including all transportation events?

What are the limits on the other as far as what is modifying we're referring to?

MS. McINTOSH: It's referring to events -

MR. EINBERG: The way I would read it, Dr. Thomadsen, and we have somebody from research here also who is responsible AO criteria and he can correct me if I'm wrong, but the way I would read this is it's events at all facilities other than nuclear power plants. And then, also, all transportation events.

VICE CHAIRMAN THOMADSEN: I would suggest clarifying that now.

MEMBER WELSH: Jim Welsh.

To follow up on Dr. Thomadsen's point, I would agree that perhaps clarifying that sentence is worthwhile. But similarly as Bruce pointed out a few minutes ago, my suggested wording perhaps needs to be wordsmithed also so as to not cause confusion as Bruce has pointed out, but also capture the spirit of what Ms. Weil's point was that you could still overdose the intended organ and have an abnormal occurrence.

So, I don't know how to wordsmith it other than perhaps putting in "or" in there and having intended dose - other than the intended dose to the intended target, or a dose other than the dose to the intended target.

CHAIRMAN MALMUD: May I try to bring the question forward in the following fashion? The first one to the Committee is does the Committee feel that it's realistic to have a single standard applicable to both nuclear medicine procedures and to radiation oncology procedures?

Dr. Langhorst.

MEMBER LANGHORST: The criteria that NRC staff is wanting to have put in place helps them to decide this medical event really doesn't need any more medical review by a physician because we know it wouldn't meet these unintended or unexpected consequences.

If we have something low enough that triggers it to catch anything, I mean, to catch what Dr. Welsh is talking about as far as the potential blindness, I would suggest that maybe for the intended target that doses greater than 50 percent more or something like that as far as what was intended and it's greater than a hundred rad to any other tissue. And that's a really sensitive criteria that then you have a physician come in and review for the red items of the unintended/unexpected results.

It's always disappointing to me that we're trying to save so much money and not having the NRC hire a lot of physicians to do these reviews when we have a lot of people who review things in a power plant situation.

I mean, I think we should have a lot of physicians looking at these particular events to see if they are of significance to report to Congress.

So, I think you can have a very sensitive number that may lead to a lot of physicians having to - consultants having to review these things, but I think that's what's needed and could be very simple and trigger that additional review by a medical professional.

CHAIRMAN MALMUD: So, you believe that it could be a single standard applicable to both nuclear

medicine procedures and radiation oncology procedures?

MEMBER LANGHORST: Yes.

MEMBER MATTMULLER: Steve Mattmuller.

I'm really struggling with the direction of our discussion today. Because as I remember past discussions on this issue, using the blue criteria and evaluating existing medical events and then taking them to the level of an AO that goes to Congress, I thought we had a pretty uniform agreement that these were too sensitive.

That if you look back at some of the past reports that go to Congress, there are really incidents that don't need to go to Congress. And, hence, that's why we try to come up with the unintended.

So, now I'm really struggling with now we're saying it's still not sensitive enough. I mean, I thought we were already in agreement that they were too sensitive.

CHAIRMAN MALMUD: Well, that was my point, Steve. You are correct. We were trying to eliminate unnecessary reports to Congress which created issues that really were trivial.

My question is, can we have such a sensitive screening that is applicable to both radiation oncology and nuclear medicine?

They're two different techniques. And within radiation oncology, there are a variety of techniques.

When people in the field have to evaluate these, they are not sophisticated - they are not necessarily sophisticated Ph.D. physicists. And, therefore, they will go by the book. And if the book says X, they're going to do X even though it may be trivial.

So, the trick is to find the standards that are a reasonable cutoff, and I'm questioning whether or not such a standard could be applied across these various disciplines. And that's the question I'm addressing and that Dr. Langhorst wants to comment on again.

MEMBER LANGHORST: Thank you. So, really the new criteria are the red listed bullets. That is the new criteria to make that an adverse occurrence.

What was used in the past, the blue bullets, NRC is asking, staff is asking this is what we want to check to see do we need to bring a medical consultant on board to then review the red bullets.

I think we need to have a low threshold for that criteria on when to bring in a medical professional to judge the red criteria that would be unintended/unexpected permanent functional damage, those criteria.

And I am sensitive to the need to save money, but I think it would be good to have medical professionals judge these criteria and have a very sensitive trigger point for staff to choose or to have exceeded to then bring in that medical professional.

CHAIRMAN MALMUD: Mr. Einberg.

MR. EINBERG: Thank you, Dr. Langhorst.

And to your point and to Dr. Welsh's point as far as that the criteria were too sensitive previously and we were trying to fix that, part of the criteria if you look - actually, can you bring up the blue criteria, the third bullet there, greater than or equal to a thousand rad to any other unintended organ, that previously we've clarified that.

It previously stated to any organ. And that was, you know, whenever you had a medical event because of the therapeutic doses, you would automatically have an AO. So, we put in "unintended organ" to clarify that to raise the threshold there. However, as per this discussion, that's had unintended consequences as well.

CHAIRMAN MALMUD: Dr. Welsh.

MEMBER WELSH: To answer your question, Dr. Malmud, I personally think that we could come up with one set of criteria that would be appropriate for both nuclear medicine, diagnostic procedures and all forms of

therapy if the nominal figures are adjusted appropriately. They would have to be decreased to capture everything, but I do think that it's possible.

I think the question, a big question, big-picture question might be which is going to be an easier task to come up with criteria for nuclear medicine, diagnostic, HDR brachytherapy, permanent implant brachytherapy, gamma knife, et cetera, et cetera, versus the solution that's currently proposed in addressing the numbers.

I personally think that we could use the proposed suggestion up on the board now and adjust the numbers far easier than the alternative of coming up with criteria for all the different modalities.

And for that reason as well as the other I have mentioned, I'm in favor of one set of criteria for both nuclear medicine and therapy.

CHAIRMAN MALMUD: Thank you. Dr. Suleiman.

MEMBER SULEIMAN: I think some systems analyst somewhere is saying, gee, this would be so easy. I think you need a systems approach to this.

This is a - you want a sensitive indicator. So, let's say the medical event criteria is adequate, but then you want to triage and pick up the really serious ones.

I don't think based on my own experience and I can give you examples, unless you get exam-specific, you're not going to be able to apply criteria across the board.

And even if you try to somehow translate that into a risk number, I wouldn't go there, I mean, to sort of standardize or normalize, because risk varies for individual.

If you've got cancer patients that all have expected lifetimes of a year, their risk of harm versus their risk of living is very different than a four-year-old child. So, risk varies, but that's, I think, what we're trying to drive here.

You're trying to come up with a dose number that sort of says, this is serious, we need to report this.

I think at triage, somehow you're using the medical event criteria. And then at that point, a decision has got to be made. I think experts in the appropriate modality have to say, this is standard of practice, this is normal, and whereas the same number may be serious for another modality.

So, I'm uncomfortable with trying to make it apply across the board to everything. I think you need to segregate somehow by modality or source.

CHAIRMAN MALMUD: Dr. Welsh.

MEMBER WELSH: Jim Welsh.

If I might reply to Dr. Suleiman's points, yes, you are correct, but I think that the red bullet points that have been added help clarify this. Because when we say permanent functional damage or significant unexpected adverse effect or death, I don't think that you have to be a health professional to recognize such severe consequences.

So, the numbers on the previous part of the boolean and, I think, are irrelevant, but could we come up with - we could come up with some numbers.

It's the important second component of this boolean and, the red bulleted added points that are the real meat of all this and permanent functional damage or death satisfies those concerns. And I don't think that you need to bring in medical experts for each and every one of these things that is more than 250 rad to the gonads, because they're not going to satisfy the other criteria in the boolean and of death or unexpected permanent functional damage.

So, I think that the added red bullet points answer that concern.

CHAIRMAN MALMUD: So, Dr. Welsh, you're in favor of the current proposal with the exception of the

doses that are stated?

MEMBER WELSH: Yes, those nominal figures are inappropriate.

CHAIRMAN MALMUD: Dr. Guiberteau.

MEMBER GUIBERTEAU: You know, I think there are two things in the screening that we deal with in diagnostic radiology. And one is the sensitivity of the study, but the other major area is the appropriateness of the screening criteria.

I think we go to great pains in the NRC and the ACMUI to address our stakeholders based on the modalities that they deal - that they use.

The medical event criteria as the initial screening criteria, apply to everyone. So, it's very general.

I think we owe it to our stakeholders and I think we need these screening criterias because unlike Jim I think once it gets to these medical issues that only a physician is qualified to deem whether they are significant or not, that puts that clearly where it belongs in the practice of medicine.

In the interim screening criteria between medical events and abnormal events based on dose if they are category-specific, would basically put this - put that part of it back where it belongs in the NRC. So, it

would tie these two together and I'm very uncomfortable trying to get not only medical event as generic criteria, and then we're trying to parse it out by another set of general criteria.

I think what will happen is that in nuclear medicine, some things will, you know, we're going to have to have them pretty low to catch some of our things. And the same is true with radiation oncology.

And what I don't want to deal with is, for instance, in my case, the nuclear radiology, you know, stakeholders saying, well, you know, all of these things are being captured because we have one set of criteria. And it's, you know, it's too low for really - it's capturing a lot of things we don't need.

So, I mean, I do understand it would be nice to do that, but I think the process here is winnowing out. And in order to winnow out, we go from the general criteria of a medical event and parse this out based on the secondary criteria, and then get to the medical issues. To me, that makes perfect sense.

MS. McINTOSH: Dr. Malmud.

CHAIRMAN MALMUD: Thank you, Ms. McIntosh.

MS. McINTOSH: I appreciate that comment, Dr. Guiberteau. And I realize that this committee is here to help us, you know, with regard to identifying what is

- or that the medical aspect of it is your - is primarily what will always be your focus.

But I do want to also reiterate along with Dr. Guiberteau's comment, that we are in an environment where we're trying to be open as possible, because we are told we have to be. And part of that openness is reporting things as promptly as we possibly can and in a timely, you know, in a timely manner.

So, from the staff's perspective, it would be helpful for us to have some common sense kind of criteria that will help us to relatively quickly identify things for screening so that they are promptly reported to Congress, you know, unless the NRC is accused of, you know, withholding information and that sort of thing.

And also we recognize that we are not physicians and we don't want to be put in a position where the criteria are so general that we're sort of making these medical judgments.

We would prefer that, you know, things be parsed out for us enough that just with our HP and engineering backgrounds we can decipher that event enough to say it makes sense for this event to be sent to a consultant. And we get that done in, like I was saying, a timely manner to satisfy our stakeholders' concerns of being informed promptly of things.

So, I'm just throwing out for consideration as well.

CHAIRMAN MALMUD: Thank you. We understand the goal. We're trying to assist you in achieving it, and obviously we have differing opinions within the Committee at the moment.

Dr. Langhorst.

MEMBER LANGHORST: I wanted to ask a question of you. So, you feel with this openness, that you really do need to have your screening criteria as part of this whole description and how NRC staff decides to go seek medical professional opinion; is that correct?

MS. McINTOSH: We believe it's an approach to helping us to meet that goal.

MEMBER LANGHORST: And it needs to be part of this definition and not part of this is the screening we do.

MS. McINTOSH: Well, no. I guess what I'm - the point that I was trying to make with the openness comment is that NRC is not perceived as unduly withholding information just because it's taken us so long to get these events reported to Congress.

I mean, we do have a time frame to get them, you know, an event that happens this year, maybe it kind of looks odd if it's not reported to Congress until three

years later because we had to always hire a medical consultant.

I just throw that out for consideration.

MEMBER LANGHORST: And so, I'm still not clear. Does it need to be part of the AO definition, or can it be these are the criteria that NRC staff have established to then seek medical - a medical consultant to judge the red bulleted items that are the definition for an adverse occurrence?

MR. EINBERG: To answer your question, Dr. Langhorst, I'm not sure whether it will need to be out in the open or if this is more of a procedural issue that we use to get a medical consultant to further that threshold.

My personal belief is that I'd rather have more things out in the open than, you know, have it transparent and we have people comment on it. But having said that, I'm not sure whether, you know, it's a requirement or not.

MEMBER LANGHORST: Okay. Well, I guess my point is, is, I mean, it still can be out in the open. It sounds like this definition is difficult to change because of all the logistics of doing what you've described in your next steps. And it's kind of tied to all adverse occurrences.

You have to time it with the reactor adverse occurrences when you make those changes. Am I correct in that?

MR. EINBERG: The abnormal occurrence of definitions or the policies, yeah, there's a paper. It's for the entire agency where -

MEMBER LANGHORST: Okay. So, I might suggest that NRC can still remain open by having its guidance on its criteria that they know needs more medical review on judging the red bulleted items, that then gives you some flexibility of adjusting those criteria as you learn more going through what is a true abnormal occurrence or what is a significant abnormal occurrence. And that might be easier to change going forward rather than being part of the actual definition of adverse occurrence.

CHAIRMAN MALMUD: You wish to comment on that, Mr. Einberg?

MR. EINBERG: I think that's certainly an approach. I would have to explore it with our different offices and our Office of General Counsel to see whether that's achievable or not.

The one thought I do have in those regards is that, you know, the NRC would have their screening criteria, but then each Agreement State would have to have a separate screening criteria or they would have

their own screening criteria. Which, you know, there could be all these different screening criteria out there, and so that's - from a practical standpoint, it would be better to have one and have that all discussed.

CHAIRMAN MALMUD: Ms. Bailey.

MEMBER BAILEY: I may be confused, but I think when we get to abnormal occurrences there is the report to Congress; NRC has that role with the states. I mean, we've entered our medical events and, yes, we're going to communicate, well, here's what happened and we may come to the decision, it would be NRC's criteria that develop the report to Congress.

MR. EINBERG: Well, if -

MEMBER BAILEY: - it went into the report to Congress.

MR. EINBERG: The criteria that is being proposed now is just to have the criteria that's in the red then.

MEMBER BAILEY: Right.

MR. EINBERG: But as far as making that determination, then I guess we're discussing whose role would it be to make that determination whether it's significant or, yeah.

MEMBER BAILEY: And I think routinely we would all work - we and NRC would come together. Because

routinely, NRC has come into our space at that point and go on and why do you think this is not an abnormal occurrence or why do you think it is.

So, I don't know that we would necessarily have different screening criteria.

MR. EINBERG: Okay.

MEMBER BAILEY: I believe you would have a role and say, yeah.

MR. EINBERG: Okay.

MEMBER BAILEY: I think, at that point.

MR. EINBERG: Okay. Thank you, Ms. Bailey.

CHAIRMAN MALMUD: Another issue which hasn't been discussed is that - it's been alluded to is that our responsibility to our stakeholders, including the providers of these services, the requirement for a physician or physicist to review a case will create anxiety within the department that's being looked at.

And if the criteria are too sensitive, that's going to create an atmosphere in which there may be given human behavior, a desire not to reveal events.

Once again I come back to the issue which I won't give up on mentioning, although I may be defeated on it in the Committee, and that is I don't believe that these criteria are uniformly applicable across the various specialties in radiology in the use of

radioactive material.

And to make them too sensitive so that they are fair to one specialty and unfair to another is a mistake. Whereas if they are defined in a handbook and guidance to our people out in the field, they'll know what to do.

When I was in the military, they used to say the best training manuals were written by geniuses for the Navy to be used by less than geniuses. And I would make an analogy here in that it's the responsibility of NRC and this committee in its consulting role, to devise the best criterion possible so that they can be applied by people who are not as highly trained as members of this committee are.

And we miss that point when we assume that they're going to have the same ability to make a wise decision as some of you, and that they have the ability to do that. They need guidelines.

I don't see a uniform guideline. Dr. Welsh does, and he and I differ on this point, because he comes from one specialty, and I from another.

Dr. Welsh.

MEMBER WELSH: Jim Welsh.

If I might respond to continue the debate with your perspective and with Dr. Guiberteau's, I would

go back to the question that you raised earlier about how often does a diagnostic nuclear medicine procedure ever get elevated to the point of abnormal occurrence.

And I think I heard earlier the answer is screen the rarely, if not zero, and that might be in part because of those new red bulleted items such as death and permanent damage.

And if I'm correct in this interpretation, it doesn't matter what the previous component of that boolean and is. Those numbers could be anything. It doesn't matter if they were - the numbers were zero, because if you don't get death and unintended permanent damage from a diagnostic procedure, you will never have inappropriately low or an unduly sensitive definition for abnormal occurrence that would adversely affect the nuclear medicine diagnostic community.

CHAIRMAN MALMUD: I accept your point.

Dr. Suleiman.

MEMBER SULEIMAN: Really, I don't want to say what I'm going to say, but I will, okay.

(Laughter.)

MEMBER SULEIMAN: I don't want to introduce risk. I told everybody we shouldn't be discussing it. But if you administer a diagnostic dose that's a thousand times what they should have got, you may not see

short-term deterministic harm, but you've clearly increased the risk of that individual.

How do you weigh that? I mean, I'm asking you. So, is that any less important than maybe giving an extra several gray to a therapy patient?

So, I wouldn't - the problem is we consider diagnostics so safe that the community sometimes gets pretty flippant and sloppy about how they use diagnostic procedures. I mean, that's my perspective.

The community they are diagnostic, we don't worry about that, but we've seen at least with machine-produced equipment where you actually get skin burns or necrosis and you get hair loss. And so, it's capable.

So, sorry, Dr. Malmud, I agree with you a hundred percent. You have all these guidelines for different diseases and you look at it and you find out what the state of the practice is, and medicine is fuzzy.

So, what's pretty precise and limiting in one area and I'm going to use external radiation therapy, may be completely inappropriate for some of the other things.

So, trying to have one size fits all, one number fits all, is why we're dealing with this thing right now.

I think you need a triage. I don't think you need medical analysis earlier on. I think the final analysis will be when you've got this very specific procedure and the hospital as the institutions, the site should be evaluating these errors or mistakes on a case by case.

But the purpose of the NRC just like the purpose of the FDA is, are we seeing a trend here? Is this broader than just this isolated incident? Should we do something?

I mean, aside from reporting to Congress whatever, you know, all statutes have that requirement. So, when I first started government I said, wow. Then I find out that every statute says you have to let us know what's going on, but I think clearly you can't just be collecting information and not passing it on.

But at some point you may not need expensive review early on, but only if it's simple so you can do the analysis. But as I said, I look at this thing and I get confused. How am I going to interpret this? How am I going to apply it?

But if it was different modalities, you could probably come up with some pretty simple numbers that you could have cutoffs for.

And then finally the physicians will weight

in and say this is appropriate or this is not appropriate.

CHAIRMAN MALMUD: Thank you. Dr. Langhorst.

MEMBER LANGHORST: I think you can have one criteria for all if it has to be part of this formal definition that can only be changed every so often.

I'm uncomfortable with trying to do specific therapy numbers in a definition that can't change often.

So, really, adverse occurrence are the red bulleted items. And I think that if NRC needs some criteria on who, when to bring in that medical professional, I think that should be as you've been calling it, Dr. Malmud, guidance. It shouldn't be part of this definition.

But if we have to have criteria to be part of this definition, I think we want a very sensitive one, very simple one that then brings in the medical professional to decide the red bulleted items.

CHAIRMAN MALMUD: Thank you. Dr. Welsh.

MEMBER WELSH: Jim Welsh.

If I might respond to Dr. Suleiman's point, I think that even if we try to come up with separate criteria for each one of the modalities or diagnostic procedures, we're still going to wind up pretty much where we are now, but maybe with different numbers.

Because I think Orhan's point was maybe stochastic events from a nuclear medicine procedure in which the dose was via the administered activity, was a thousand times off, could result in an adverse health effect such as a stochastic rather than these deterministic effects that we're classically thinking of.

However, bullet point Number 3 is significant unexpected adverse health effect, which I believe would include any of these stochastic events also.

So, there is inherently going to be some medical judgment in this whole process of abnormal occurrence definition, but I don't believe that the extra - and I think significant extra effort of trying to come up with different categories for each one of the different modalities is an exercise that's really worthwhile in the long run because we're going to come up with the same solution in the end, I think, for everything.

CHAIRMAN MALMUD: Thank you. I also thought that Dr. Langhorst's point that these numbers will change with time as new procedures are introduced and, therefore, these numbers will need to be reevaluated periodically is a very valid one.

And we'll need to back off of my point based upon the argument presented by Dr. Langhorst and the - your willingness to apply the current criteria to radiation oncology procedures.

Mr. Einberg.

MR. EINBERG: One possibility, if I may suggest, is to have a subcommittee formed to decide what those numbers should be. And then we'll take the action from our standpoint to determine whether we can point, you know, use that screening criteria from an administrator's standpoint or whether it has to be in a more formal abnormal occurrence process.

We'll still need some kind of screening for everything - we're still - I think what I'm hearing is we're going in the direction that we need some kind of screening criteria whether it be modality specific or not. But perhaps a subcommittee could hash that and then provide something to the NRC staff.

And then we'll take that and either put it into the formal abnormal occurrence process, or we'll put it into some kind of a handbook or into one of our administrative procedures for using that to screen whether we get a medical consultant or not.

CHAIRMAN MALMUD: Thank you. Dr. Suleiman.

MEMBER SULEIMAN: Let me ask a question that

we, both agencies, have dealt with the last year. But when a patient gets a radiopharmaceutical and the amount of activity that they've received, the dose that they've received may be 40 or 50 times that which they were supposed to receive, and in some cases some of these patients, this is number of patients are subject - there are some issues there whether it's with the user or manufacturing or both, but some of them, in fact, may have received more than, you know, five millisieverts, five rads or higher, because the dose estimates by experts say we could be off by two or three in either direction. So, they could be getting much more than five or 10 rads or lower.

Would that qualify as an abnormal occurrence, or is that just a product mislabeling - is that serious enough to -

CHAIRMAN MALMUD: To whom is your question addressed?

MEMBER SULEIMAN: Anybody. To NRC.

MR. EINBERG: That's under the existing abnormal occurrence, or the new proposed AO criteria?

MEMBER SULEIMAN: Both. Would it fall under one, and not the other?

MS. McINTOSH: Under the current criteria if it's not one of these listed organs, bone marrow, gonads,

so on and so forth, it has to be at least a thousand above what was prescribed.

If it's one of those targets, it has to be what the target specifies there, a hundred rad to the bone marrow or lens of the eye or 250 to the gonads.

Under the new criteria, it wouldn't - it would have to be unintended permanent functional damage would have one of those unintended statements or significant adverse health effect things would have to have occurred.

MS. HENDERSON: Under either of the criteria it would not be an AO, because it's not triggering the doses.

CHAIRMAN MALMUD: Okay, thank you. I think Dr. Welsh had his hand up next.

MEMBER WELSH: And my point is that, yes, that that's correct. It would not be an abnormal occurrence, and it should not be.

Because in my understanding, the abnormal occurrence is way at the top of the list as the worst possible scenario, and this does not qualify for that. And I don't think too many diagnostic procedures ever are elevated to that severity that they would or should meet any existing or proposed definition.

MS. HENDERSON: I mean, that doesn't mean we

wouldn't capture it under medical event and that there could be a big programmatic problem that caused the medical event. So, it would still be looked at.

MEMBER SULEIMAN: I mean, that's sort of how it's played out.

MS. HENDERSON: Yes, yes, uh-huh.

CHAIRMAN MALMUD: Mr. Mattmuller.

MEMBER MATTMULLER: This would be to the staff. Was it your intention with retaining the blue criteria, that that would be the trigger point as to when you would have a physician review the case to see if then the red points apply?

MR. EINBERG: That's correct.

MEMBER MATTMULLER: Okay.

CHAIRMAN MALMUD: Thank you. Now, is the Committee prepared to vote on this document as amended at the current time?

Ms. Weil.

MEMBER WEIL: In the interest of wordsmithing, I would just like to suggest that unintended and unexpected might be better unintended or unexpected.

Dr. Welsh, is that what you were after when you suggested that? Does it need to -

MEMBER WELSH: Yes, yes.

MEMBER WEIL: Okay. So, it should be an "or". Okay.

And then if we could go back one to the first statement, a medical event that results in - this is back in my original point. Could we say an unintended dose to the intended target - that's ugly - or then the phrase that is there, a dose other than the dose to the intended target that is.

That's not particularly elegant, but I think it needs to be an "or". I think we need to have one statement that refers to the intended target, and one statement that refers to unintended target.

CHAIRMAN MALMUD: Dr. Thomadsen.

VICE CHAIRMAN THOMADSEN: I'm still unclear as to why.

MEMBER WEIL: Because you think it's a medical event and - it just seems to me that this language is so exclusive of intended targets that it is misleading.

VICE CHAIRMAN THOMADSEN: Yes, but why do we care if the target gets more dose? We had a medical event with Zevalin where the patient received - I think it was 50 percent more dose than they should have, according to the description. Actually, the disease disappeared. They had no other problems to any other organs in their body,

because the doses would not have triggered any of that. But that would have been an abnormal event, but actually was a beneficial event.

Why do we care?

CHAIRMAN MALMUD: Dr. Welsh.

MEMBER WELSH: I'm going to contradict myself because thanks to your question or comment I've come up with the example in nuclear medicine diagnostics where you can have possibly an abnormal occurrence. And that is diagnostic procedure for thyroid cancer, in which case you would want to diagnose - make a - with thyroid disease. A diagnostic procedure for thyroid disease in which the dose was so off that you ablated the entire thyroid inadvertently.

And for that reason, I think that Ms. Weil's point is important that it can be the intended target. But if the intended dose is way, way off, you can have an abnormal occurrence.

That's why as inelegant or ugly as that wording is, it's to the point that I think that it's worth rewording it.

CHAIRMAN MALMUD: Except that one of the risks of I-131 therapy to the thyroid is ablation. Unintentional ablation is a risk, because the thyroid has variable radiosensitivity.

So, even though the dose may be very carefully calculated, in a particular patient it may result in ablation.

Dr. Welsh.

MEMBER WELSH: If the isotope was I-123 for diagnostic procedure and the isotope was I-131 and it was the incorrect activity, you could have -

CHAIRMAN MALMUD: That's clearly a misadministration. It's the wrong radiopharmaceutical.

MEMBER WELSH: It's a medical event misadministration and it would perhaps fall into this category.

CHAIRMAN MALMUD: Yeah, I agree. Dr. Suleiman.

MEMBER SULEIMAN: All right. I remember a couple of years ago at a Society of Nuclear Medicine meeting where one of the physicians gave a talk. And the first thing he says, I don't want to disappoint you all, but we give every patient 150 millicuries per thyroid ablation. End of discussion.

And so, ever since then I sort of ask my nuclear medicine colleagues, what do you use? Some do the dosimetry, and some don't.

That tells me that the practice of medicine, of therapeutic, there may be some that are doing it one

way, and there may be others that are doing it another way, but I think that's still being sorted out among the medical community. So, it's medical practice until the professionals all decide you should be doing it, you know, this way.

Which gets back to the fuzzy standards. What's acceptable for one group? I mean, at some point you have to kick it over to the medical community and say, this is standard of care, this is standard of practice. And so, we're going to have this fuzzy line as to what's appropriate or not.

With the therapeutic I think especially with the particulates maybe if you overdose, there's nothing wrong with it. So, you give it up, so, as long as you're making sure you're not falling below that threshold.

There are just so many complex issues that one number - and then you've got the uncertainty, you know. You have one person say, well, we've exceeded the limit, and some other person will say, no, it's up by a factor of two.

FEMALE PARTICIPANT: See if this works.

CHAIRMAN MALMUD: Ms. Weil.

MEMBER WEIL: To the point that was made earlier that thyroids are radiosensitive in different

ways, an unintended dose to the target, not the intended dose that behaved peculiarly, but an unintended dose to the target, or take out the - actually the green intended.

So, it's just adding that small phrase to the beginning, which then would be inclusive of unintended doses to the target organ, not eliminating them and saying only doses that are other than the intended target.

Does that make sense?

CHAIRMAN MALMUD: Dr. Thomadsen.

VICE CHAIRMAN THOMADSEN: Well, according to that, then, all medical events in which there is an unintended dose to the target, that is the target receiving more than 20 percent, would be an abnormal event.

MEMBER WEIL: Only if it met the other red criteria at the bottom.

VICE CHAIRMAN THOMADSEN: That doesn't seem to be what that was saying.

(Discussion off the record.)

MS. McINTOSH: We do intend that the unintended permanent functional damage, one of those statements, also be met.

VICE CHAIRMAN THOMADSEN: In that case, the or after the target maybe should be an "and".

(Simultaneous speaking.)

VICE CHAIRMAN THOMADSEN: Right.

MS. McINTOSH: This was screened for us, and then we would look at this.

VICE CHAIRMAN THOMADSEN: Yeah, and I'm not sure that that's actually capturing that.

CHAIRMAN MALMUD: Ms. Henderson.

MS. HENDERSON: May I suggest that this really does need to be addressed by a subcommittee. That we're doing a workshop here and wordsmithing and that we really need to take the time to look at this very closely and it's not going to happen in the time frame we have today.

CHAIRMAN MALMUD: I think most of us agree that there's clearly a lack of consensus here with regard to the current document. We understand the goal, but we haven't achieved it yet and it should go back to a subcommittee.

I motion for further clarification and then representation to this. Do we all agree that we can do that? There is agreement. Thank you for the recommendation.

And, Angela, than you for putting together a very difficult document, but a very sound one in terms of where we need to go from here. Thank you.

MS. McINTOSH: Thank you, Dr. Malmud.

CHAIRMAN MALMUD: Mr. Einberg.

MR. EINBERG: I assume that you'll form a subcommittee at this point then?

CHAIRMAN MALMUD: Yes. Does anyone wish to volunteer to chair this subcommittee?

(No response.)

(Laughter.)

CHAIRMAN MALMUD: I think Dr. Langhorst, Dr. Welsh and Dr. Thomadsen have demonstrated intense interest in this, as has Dr. Suleiman. But I'm standing on the left side of the table, and Dr. Palestro's silence has been deafening.

(Laughter.)

CHAIRMAN MALMUD: And I know that you have something to say.

MEMBER PALESTRO: I'll be happy to work on the subcommittee.

CHAIRMAN MALMUD: Thank you. And Ms. Weil. Okay. So, that's the committee. Dr. Langhorst is the chair, Ms. Weil, Dr. Palestro, Dr. Thomadsen. And then on this side of the table we have with Dr. Langhorst, we have Dr. Welsh.

MR. EINBERG: Dr. Malmud, I'd like to also offer an NRC staff resource to the committee, and that

would be Angela.

CHAIRMAN MALMUD: Thank you.

MR. EINBERG: I think that is - in previous subcommittees, that's been very useful to have a staff resource who can answer questions on various aspects.

I would also perhaps recommend that Ms. Bailey be considered for the subcommittee, because it does have implications for the states.

CHAIRMAN MALMUD: All right, thank you. Oh, Dr. Langhorst.

MEMBER LANGHORST: I would ask one more thing. I would definitely ask the NRC staff to give the subcommittee their conclusion on whether criteria needs to be part of the definition, or whether it can be removed from that and obviously publicly shared, but not be part of the definition of adverse occurrence. That would be greatly helpful to our subcommittee.

MR. EINBERG: Okay, absolutely we'll do that. And then also, Ashley, if you could send Dr. Langhorst the wordsmith edits as a starting point, you know, we've done some work on those and that might be a good place to start with.

CHAIRMAN MALMUD: And with that, we will take a break.Can we get back at 10:30? Thank you.

(Whereupon, the above-entitled matter went

off the record at 10:12 a.m. and resumed at 10:31 a.m.)

CHAIRMAN MALMUD: We'll begin with a presentation by Mr. Cool, "Reducing Occupational Dose Limits." And he will discuss the potential changes to 10 CFR Parts 20 and 50. Thank you - excuse me, I stand corrected. Dr. Cool.

DR. COOL: Good morning, ladies and gentlemen. It's good to be back and see a number of you that I have known for many years and appreciated the relationship.

It turns out that the last time we talked about this subject was actually October of 2010. So, it's been a little while.

So, what I intend to do today is to give you just a very quick, full update for those who haven't touched this subject of late, and then to review the information that is in the staff's SECY paper.

So, by way of background, the NRC regulations for radiation protection derive their bases from national and international recommendations, use as points of reference for its international standards, use both national and international analyses of health effects, radiation risks, as well as reflect an ongoing coordination with various federal and the state agencies.

The last time 10 CFR Part 20, which is referred to as "Part 20" most of the time, was significantly revised was 1991. That was the culmination of a 12-year process of revision, substantial revision, and actually had its basis in the then new ICRP recommendations, Publication 26 from 1977.

Other portions of the regulations which were not cross-references as in they contained their own explicit dose criteria or references, were not updated at that time. So, in fact, part of the issue that we have is that you have within the NRC regulation guidance structure three new generations of recommendations and scientific information going all the way back to 1958 and `59.

ICRP completed their latest revision update of their recommendations in December of 2007. ICRP Publication 103.

The staff as we had committed to our commission did an analysis, which we presented to them in December of 2008 indicating that there were some areas that certainly warranted an examination for possible updates.

The Commission approved us going off and beginning to engage the stakeholders and initiating for development of technical basis information in April

2009. We have been busy doing that since that point.

A set of recommendations in a staff paper was provided to the Commission on April 25th of this year, and that's what I will be reviewing for you.

Over the last three years we have done a lot of different things to try and reach out to various stakeholder organizations. We've had interactions with this committee on at least three occasions, with the Advisory Committee on Reactor Safeguards, with a wide variety of organizations, professional societies, groups and otherwise the organization of agreement states, conference of radiation control program directors.

Federal Register Notices put out there. We all know that everyone reads the FR, but that's the way in which we can actually formally develop a docket and keep track of all the things for nice, legal purposes.

We ran a series of three more formal facilitated roundtable workshops where if you take this table and make it about three times as large, you put 30 something people around it representing every kind of licensed use that we have, plus some other stakeholders and get them all to talk about this subject, you have sort of a rough idea of what those two to three days worth of activities were. They were quite enlightening.

The workshop in Los Angeles was specifically aimed towards medical uses. More than half the participants were from the wide variety of different medial uses. Several of you here participated in those workshops.

In addition to that, there was a called third phase after the ICRP put out a separate new recommendation related to protection for lens of the eye, which was last year.

We had a total of 59 formal comments on the docket. From the 500,000-foot level there was general support for the idea of doing some updates, updating methodologies and terminologies.

There was also equally a generalized view that we should just say "no" to changes to the actual regulations, dose limits, ALARA, those sorts of things. A view, unfortunately, not substantiated by detailed discussions despite our attempts to elicit them with regards to the risks, generalized statements that the impact would be unacceptable that you would no longer be able to practice medicine, you'd no longer be able to do industrial radiography, et cetera, and the number of times where there was a view expressed that the kinds of sources that are used in the United States as in typically somewhat higher activities than that used in Europe,

meant that we should have different dose limits applicable to us. That's a view.

So, to briefly review where some of the pieces are, radiation risk. The current basis for the regulations, as I said, is a mixture from 1958 to 1990. Part 20 itself in basis, is based on what was known in the late 1970s as in one times 10 to the minus four per rem cancer mortality and risk of heritable disease.

Now, that's not the number that we are all familiarity with. Because by the time the rule was finalized in 1991, there had been updates to the dosimetry in Hiroshima/Nagasaki, there were considerable additional follow-ups with that cohort and other cohorts and the general presumptive risk for radiation was more like five times to the minus four per rem.

In addition, there was a broadening consideration of not just cancer mortality, but morbidity, years of life lost and other things as they looked at the risk. And that's all discussed in a moment in the methodology.

The most recent analysis is actually from EPA, EPA's radiogenic cancer risk models and projections for the US population, which was published in April of 2011. Their value for incidence, 1.2 time 10 to the minus

three per rem of radiation. Cancer mortality, 5.8 times 10 to the minus four with the range on that latter number being 2.8 times 10 to the minus four to one times 10 to the minus three.

And so, while if you look at the risk estimates and you look at the ranges of risk that are associated with each of those, those uncertainty bands clearly overlap. In fact, the current uncertainty band does not include the central estimate of the previous band.

Methodological basis, again, we have a wide variety of things. You've got some parts such as Part 50, Appendix I, which is the ALARA effluent for reactors, some of the things related to sources in Part 30 and other things, which go all the way back to `58 and `59, critical organ concept, a system which did not allow the summation for internal and external exposures.

Part 20 generally based on Publication 26 and 30, total effect of dose equivalent approach, some also now use the ICRP 60 methodology. The Commission has by specific license amendment, authorized the licensee to use the new set of methodologies that came out in the early `90s for a licensee so long as they use that entire set. And so, they couldn't cherry pick new and old numbers, whichever they thought would be more

advantageous for them.

The public exposure limits in Part 20 actually reflect the new risk estimates, because the proposals at the time that rule was a proposed rule included within the range of options, the current recommendation for a public dose limit of 100 millirem a year.

The occupational numbers do not, because the proposals that were out at that time did not include the recommendations for lowering the occupational dose limit in light of the revised radiation risks. And there was nothing upon which we could base a change.

The staff, in fact, in the statement of considerations noted the publication, the ICRP recommendations, and noted that at that time that the change was not substantial enough to warrant stopping the presses, those aren't actually the words used, but that's an easier way to express it, because of the significant changes and reductions that were already being made and the importance of getting that out and getting it implemented and would be revisited later.

So, in addition to that, something which actually becomes fairly important in some of the medical modalities at the time in 1991 that the rule was published, the external dose was measured by the mean

dose equivalent as in the badge at the point of highest exposure on the body.

The modeling in approaches and considerations have of course continued to improve. And the NRC regulation today now recognizes effective dose from external exposure allowing for several different standard methodologies for calculating an effective dose from one or more badges when there is known geometries shielding to the body such as the leaded aprons in interventional radiology and cardiology, which substantially reduces the effective dose on an individual vis-a-vis that which would be the badge on the collar up above the lead apron.

The basis for the occupational dose limits in 1977 wanted to have protection be roughly equivalent to that which was generally accepted for a safe working environment. Roughly, 1.3 to the minus four risk.

That risk actually corresponded not to the limit selected, but to the limits and the assumption that the application of the as low as reasonably achievable principle would result in essentially everyone getting a fraction of that as in one rem.

So, the actual numeric equivalence to generally accepted working environment was one rem, not five rem.

ICRP's recommendations in 1990 adopted a considerably more complex multi-attribute approach. I won't attempt to describe to you all of the considerations that went into that, but you can enjoy reading the first appendix of ICRP Publication 60 if you're having a little bit of insomnia and wish to go into those details from that time. That has essentially not changed since that point.

ICRP's new recommendations did not change the occupational dose limits. They still recommend an average of two rem per year over a five-year period, or sometimes expressed as 10 rem over five years, with a maximum of five in any one year.

Underlying that, the basis is a basis that it is not acceptable to have a cumulative exposure over the working lifetime of an individual to be greater than one sievert, or 100 rem. That is actually the same underlying basis which is the support for the NCRP, the National Council on Radiation Protection and Measurement's recommendation.

NCRP chose a slightly different recommended approach. They said five in any one year, but that an individual's cumulative should be limited to one times N their age in years.

And you can see that that has different

implications over the course of time depending on how you might accumulate exposure.

I should also note that the Commission in putting out the revision of Part 20 in 1991, explicitly stated that it considered and had rejected the concept of imposing a lifetime dose limit because of a number of complications associated with the tracking follow-up and the implications for individuals.

So, to quickly now walk you through some of the pieces in the SECY paper, you will find that this tracks fairly well to different paragraphs in the SECY paper.

First, a discussion of the updated dose assessment methodology. There was general support for incorporating the latest scientific information and modeling. We've gotten a lot more refined in how we model the intake and movement of radioactive material on the body, how do you calculate the doses. We are well beyond the old phantoms, which were the nice geometric cylinders and cones, to now the voxel phantoms with more critical detail and transfer back and forth.

Those are in the process of being utilized along with the most recent revisions to nuclear decay data to prepare a new set of dose coefficients, which would be the information necessary to calculate the

annual limits of intake and derived air concentrations that would be part of Appendix B.

So, the stakeholders said, yes, we think you should go ahead and use those. Yes, we think you should go ahead and take the time necessary to have the new information, do it once, leapfrog the generation in the middle, and bring everything up to date.

And, oh, by the way, Don, can NRC see if you can get the other federal agencies to come along with you? The difficult takes a bit longer.

Terminology. With the changes in the calculation approaches came a change in how the dose was described as the new term. Current rule talks about total effective dose equivalent.

Actually, that phase was something we created, because the ICRP including their recommendation, dah, dah, dah, used the entire long sentence of the sum of dah, dah, dah, dah, dah, dah, dah, dah. And you can't do that when you write a rule and write that long paragraph every single time.

Our friends in the General Counsel's Office suggested to us, I think quite rightly, you need to have a term and stick with it so there's a definition. So, we created that.

Interestingly, everybody picked it all up.

Even ICRP now uses the phrase with the newer terminology, which is effective dose.

So, often times you will see in ICRP documents now, the reference to the limit as the limit to total effective dose. The sum of the internal and the external component.

They drop the equivalent when the calculation changed from using quality factors to describe the effects of different types of radiation, gamma, beta, to the use of the radiation weighting factor. So, there was a change in the methodological calculation with the terminology.

Everyone said, yeah, it's correct you should probably do it so that we're all using the same language. Although, it's going to be really hard to explain to all the people we've trained all the years, that total effective dose really is sort of the same thing as total effective dose equivalent and we're changing all of this and we're changing all the procedures because it's the correct term.

Okay. What we suggested to the Commission is that that should be updated and that we should look at ways to provide some flexibility so that instead of making everybody just, snap, change a bunch of things, that we allow for time so that as people update procedures

and activities, they can incorporate this into it and, therefore, reduce the burdens of moving forward.

The occupational dose limits, the one that everyone seems to focus on, the occupational dose limit does not have its basis in the current radiation risk projections.

In fact, from a legal perspective, you can accumulate doses at five rem per year every single year and be within the regulation.

Now, the total framework which also requires that exposures be reduced as low as reasonably achievable, additional words on that, means we would be really unhappy with that. But, in fact, it allows a situation in which individuals could accumulate exposures in 20 years, which would exceed the recommended cumulative level.

And, therefore, cause them to question whether or not some change should be made in order to provide a more explicit assurance that each individual would be provided protection in addition to the fact that the application of ALARA provides protection and moves the majority of the population to well below that dose limit.

The recommendations of both ICRP and NCRP have flexibility built in, because this is not a precise

number. Nothing dramatically changes at 99.9 versus a hundred in accumulation, or at two rem a year versus 2.1 or 2.2 rem a year. They are all dots on the regulatory straight line that is drawn for purposes of constructing regulation.

For the more we know there are differences in population, differences in each of us, my risk is different from Dr. Zanzonico's risk, et cetera, et cetera, et cetera. We're all different.

When I was talking with Dr. Mike Lang the other day, he's six-foot-five. A very large individual. Substantially different organ geometries and otherwise.

So, we know that this is a population average that has to be used for radiation protection purposes. This is not an estimate of an actual individual's risk associated with it.

Occupational exposure in the United States comes from a lot of places. That yellow, big piece of the pie is something that no one takes direct control over. That's the doses that airline crews, stewardesses and other folks get as a result of flying to and fro about the earth at 30,000 feet in the cosmic radiation field the whole time.

Medical is the second largest component, almost all of which is not reportable to the NRC under

the current regulations. Well, that's interesting.

In addition to what you have, other types of activities, commercial, industrial, government, education, some of those things.

So, I put you up only one chart for interest of discussions. This is from NCRP's Report Number 160 from two years ago looking at occupational exposure. This data was derived from data received from dosimetry processors.

So, it is uncorrected data in the sense that this information may have been used to calculate an effective dose, which might well have been less than the actual badge dose.

In that circle up there on the right-hand side, you'll see doses that are greater than the currently recommended average value by ICRP of two rem per year. You'll, in fact, see values in each year that are greater than five rem per year.

Again, I can't tell you the extent to which those actually represent occupational overexposures or that which may represent badge readings which, in fact, are not a total effective number for purposes of demonstrating compliance.

If you'd like to do the math on that, you'll see that 99.57 percent of the folks in that distribution

in 2006 are less than the two rem per year average. ALARA works almost all of the time. Does a good job. And that's really where protection comes from in an operational setting.

So, stakeholder feedback. We don't like the idea of changing the regulation. We think there will be significant impacts on licensed activities and delivery of healthcare and other sorts of things.

There were numerous suggestions that changing these numbers or changing ALARA or anything else would increase the weight of noncompliance, which was intimated. Not quite allegations that we actually could follow up on, but intimated that there is noncompliance in various categories with people leaving their badges and doing other things so as not to nudge up against that occupational dose number.

And again, the statements that sources and uses are different, our sources are higher, we should have a different dose limit.

I will tell you that the staff rejects the last argument. A health and safety limit that provides adequate protection in public health and safety should have no basis in what size source you use. It should be providing protection for whatever you use.

In looking at all of this and giving you a

brief preview of the discussion I'll talk about in a minute, which is the discussions on the lowest reasonably achievable approach, the staff concluded that there would be a technical basis for considering or exploring in greater detail, I believe that's the exact words used in the recommendation of that particular section, to reduce the dose limit perhaps to two rem per year.

Within this, one of the significant discussions was stakeholders in our initial activities said, please do not impose averaging. Make us look at multiple years of exposure, go back and get people's dose histories over multiple years, keep track of it, do all of that in calculating where they can be in this particular year with all of the variables associated with it. We really don't want you to go there.

Now, I suspect that as we would go forward, we might hear some modifications of that view and they see what the alternatives might be.

In the staff paper, we have suggested to the Commission that a single number might be a more straightforward approach, but that there certainly needed to be flexibility.

One of those approaches might be the same approach which is already in place for public exposure, or in place for planned exposure situations, which is to

allow for application and approval of an additional dose amount with whatever specific conditions and go over whatever period of time might be appropriate so that you can deal with the particulars of the case as need be without imposing the burden of additional record keeping, recording and transferring things upon the entire license community.

That would tend to work pretty well for a lot of materials users who usually have no difficulty in applying for and looking at exactly what they need. And the states in discussing the proposal with them were in agreement with that. It matches their approach of liking to work with the individual licensees which they have when they have issues in order to figure out the best way to move forward and have protection.

I will tell you that the folks in our reactor community are not so enamored in this approach for a very simple reason. No chief nuclear officer of a reactor is ever going to allow his reactor to apply for an additional dose limit. That would look very bad on his INPO rating.

So, the discussion will have to continue, because there are implications on both sides of the equation.

Let's move on to some of the other issues, because we have not all that much time and I want to engage

in some discussion with you.

The lens of the eye was the most recent recommendation. The ICRP recommended a reduction from the current value which was 15 rem, 150 millisieverts in any one year, to an average maximum value.

This was based on considerable evidence that has been accumulating that the threshold for cataract induction was more on the order of 50 rem accumulated dose in the lens of the eye. Substantially less than the several hundred that had been previously estimated.

Numerically, that would mean with the ICRP's recommendation of using two rem lens dose equivalent average over a five-year period and five rem maximum, that the numeric number is exactly the same as the numeric numbers for effective dose of a whole body.

Now, in many circumstances or most generalized circumstances, the effective dose and the lens dose will be similar. Not exactly the same, because there are differences in the criteria. But you will also recognize that if there are situations in which there is shielding to portions of the body such as the leaded aprons, or you have lower energy beta/gammas or very specific things or fields, that you can have substantial differences.

And that, in fact, in some cases that would make the lens of the eye the limiting dose limit for the circumstance, which it essentially has never been in the regulations to date.

I will tell you that this recommendation from ICRP has already been incorporated by the International Atomic Energy Agency and the International Basic Safety Standards, which was approved by IAE's board of governors just a year ago.

IAEA will in two weeks have a technical meeting in Vienna to start looking at developing implement guidance for how they're going to do that.

We intend to have staff participate. We expect to have a couple of US dosimetry processors be present to help discuss those sorts of issues.

Certainly information that is discussed there will be useful in an ongoing dialog for ourselves.

The feedback when we put this out was actually sort of a mixture of things. There was some question to the scientific information. There was a whole bunch of questioning about whether a cataract should be considered an equivalent effect as a cancer. And there was concern about the implication of the numbers and that would be a controlling dose in certain situations.

So, the staff has actually recommended at

this point, that we explore for purposes of trying to develop a detailed technical basis, a reduction in limits, but we have not recommended a particular value.

If you look at the comments received, those would point towards a single number value at five rem suggested by several of the commenters. So, that's what's on this particular slide.

There needs to be continued dialog, because there are a lot of open questions of how you do this. The dosimetry for lens of the eye, the dosimetry when you have leaded glasses, if you have leaded glasses with side shields and a variety of other circumstances which heretofore have not been crucial in the analysis process become more so now.

Embryo/fetus, this is an application to the occupational limit for a declared pregnant individual. This is the only limit in the regulations which only applies if the individual chooses to declare it. So, it is a variable situation.

As we discussed the recommendations, there was some mixed feedback. Much of what we heard from licensees and groups were that they were able to accommodate the individuals. So, there was no substantial impact to the activities.

There were concerns expressed about the

lower value whether that might cause individuals to not declare, because they wanted to complete residency programs or otherwise. A variety of dose possibilities not unlike some of the things we've heard with the occupational dose limit itself.

We've recommended to the Commission that we continue to develop a detailed regulatory basis for reducing the limit to the 100 millirem level, which is the ICRP recommendation.

The ICRP recommendation is stated to apply only to the period after the declaration, which again is a variable highly dependent upon when the individual would choose to declare it.

And, in fact, if you construct a whole series of scenarios, in some cases would be more restrictive than the present NRC regulation, which is 500 millirem over the entire gestation period.

It could be more restrictive? It, in fact, could be less restrictive under some circumstances if she declared later, or if a fairly substantial portion of that dose had already been received before the choice to declare it.

So, there are some things that still need to be discussed and elaborated and which will directly impact what the implications would be for different

groups of licensees.

ALARA planning. ICRP's recommendations provided a significant new emphasis on a consistent use of optimization there were for the whole process of improving protection and the use of constraint.

Their term for values that are used in planning or delimiting a set of options for consideration to try and get the best achievable protection.

We had a number of proposals to add requirements to the ALARA program. In fact, I'll be quite frank with you. We started off just thinking this might well be attacked better by adding strength to ALARA, which at the moment is a generalized statement that you should reduce exposures and, in fact, is hardly ever cited against. Citations are usually against licensee's procedures or commitments rather than to the regulation.

That also has some downsides to it. First is an opposition to determine constraints. In fact, there's an opposition to any specification of a planning value in the regulation.

Quite frankly, people said, Don, if you make that a number that is de facto a limit, you might call it by some other name. But if you require us to do specific things and if we have to take actions to return to compliance, it sounds and looks and quacks just like a

limit.

So, having gone back and forth and looked at the implications, having examined some things, we actually received some specific proposals from state commenters on how to construct this, which focused on the approach that's typically in reactors, a very detailed, proceduralized process and reviews and approvals and information, all of which pretty much guarantees they're never going to be anywhere close to the limit, or the DOE approach which is a limit of five and an administrative control level in their radiation protection guide, which requires the deputy under secretary approval to exceed, meaning it doesn't happen, and concluded that we could do that. We could impose a lot of procedural burden and detail, lots and lots and check boxes. And that when it got all said and done, it would not change at all the possibility that an individual could get over whatever the planning value might be, because you could go through all of the little box - you could check all the little boxes, you could do the approval, somebody could approve it and you could happily go right through it. Because unless you require a change in the doses, you could still have the higher doses.

So, in the end, the view was that it was probably simpler and more straightforward, more

performance-based if you want to provide the protection for that small group of individuals to high dose end, you move the limit and you work with people to figure out the right way to do it.

Some of the other things out there, one that's a favored subject for the Health Physics Society, isn't it time to use SI?

Well, certainly there are a lot of people who feel that way. The scientific literature is all that way.

There is the Health Physics Physician Statement now which is just do it. Just chop it off, end of discussion. Just make everybody go ahead and do it, for which I would quietly reflect it's not nearly that simple. If it were that simple, the US would have all of our speed signs in kilometers long ago.

So, we have recommended to the Commission that this is certainly an issue that requires some additional exploration.

There is a step that would already be consistent with the NRC's metrication policy which came out in the mid-`90s, which would be to list the SI first one step in the direction.

There needs to be considerable discussion with our federal partners in the states and others who

would do this. I have heard a number of people in the states who have said, oh, we after I am dead, okay.

On the other hand, we also have observations, for example, following the Fukushima event and the incredible press coverage and interest for months and months and all the reporters going over there. All of that discussion being in millisieverts and becquerels.

A whole new viewpoint of what people are using and a real question of so, why are you still doing this and what's a rem?

So, it's time to look at it, but we are not at all convinced that it actually passes the threshold where we should actually demand a change, continued exploration needed.

Reporting of occupational exposure, another one that gets stuck sideways in lots of people's thinking.

Currently today there are seven categories of licensed activities that are required to report. That does not include any of the medical categories. Nuclear pharmacy is one of the categories, but none of the medical physician categories, et cetera, is required to report.

Further, in terms of agreement states, it's a D. They do not have to include it in terms of the

compatibility.

So, in fact, very few of the states require any reporting of occupational exposure to their organizations.

So, when you look at the data that we have available for doing this analysis and if you go looking for something that would help us understand if some individual were working in Virginia and in D.C. and in Maryland, three different regulatory jurisdictions, you would discover that you've got nothing to rely upon.

So, it certainly begs the question of whether there is a value and whether there should be a reexamination of the implications.

Now, I will be very frank with you. The energy necessary to get to a national database of anything is very substantial. It has been done in source security in tracking of sources with the money and associated focus on that post-September 11, 2001, but not without extreme handwringing.

So, this again is something that will require a lot of discussion in what are the possible ways to make progress.

So, we've suggested to the Commission we explore the options, they explore the mechanisms. We don't have a viewpoint at the moment. It's pretty clear

to us that it's not simply make everybody report their occupational exposure to the regulatory authority.

Obviously there are some categories which have such low occupational exposures that that doesn't make sense. Why should I make small gauge uses otherwise report when they can't possibly get anywhere as close to this.

On the other hand, there are a number of categories including much of what's represented by this group around this table for which there is no data unless we go licensee by licensee to mine it in terms of getting information.

In terms of the other portions of the regulations, we have recommended to the Commission that in parallel with the revision of Part 20, that we step up and move forward with the development of the revision for Part 50, Appendix I. Move that out of the really old maximal permissible concentration approach. Have it parallel to current recommendations.

And that, in fact, as we pursue rulemaking in other areas where the older dosimetry and standards occur to look to bring those forward as a policy direction to move forward. We think that's an appropriate approach. It will take some time, of course.

As I said, much of the scientific

information for calculating internal exposures is not yet available. In fact, the complete set of revised dose coefficients from ICRP is not expected to be done until the end of 2015. So, there is still some time.

Now, while it doesn't apply to medical, Part 20 applies to everything and, thus, is subject to the backfit requirements for reactors and for fuel cycle and for several other types of facilities that have that requirement put in place.

The previous revision was justified as a substantial increase to public health and safety on both quantitative and qualitative grounds.

I think you can readily see that there are some things where you cannot do a dollar per person rem improvement to justify making a change, but that there are a variety of other reasons which may make that the right thing to do. Those are the qualitative grounds that we put in place.

Things such as a change in dose limit could be argued under the grounds of a redefinition of adequate protection. That would have to be worked through in each of the individual basis to put together the particular case once we know what the proposal might be.

So, don't let my statement here suggest that that would or would not be used, or how it would be

constructed. It very much depends on the details of the proposal.

So, that means that we need a lot of additional information. It's really hard to generate specifics of the regulatory analysis, cost benefit analysis when you're discussing concepts. It only works if you actually are talking about the specifics of the impacts, what might the language actually look like. What might be the approach for compliance as in the general approach to the guidance.

The staff has recommended to the Commission that we believe that there's a sufficient basis to warrant the continued expenditure of our resources to develop the details to work through with the stakeholders the possible implications so as to develop that regulatory basis, the technical basis for each of these areas and bring it back to the Commission.

We have not recommended to the Commission that this is the final decision on any of those things. Details to follow. Clearly we expect some renewed discussion on what's the right kind of flexibility, because one size does not fit all.

And we're recommended to them that they approve that the staff continue to move forward in parallel that with the regulatory basis for doing Part

50, Appendix I.

With that, ladies and gentlemen, I am concluded with this walk-through of that and I will be pleased to answer your questions. Thank you very much.

CHAIRMAN MALMUD: Thank you, Dr. Cool.

Are there questions for Dr. Cool? Very thorough presentation.

Dr. Zanzonico.

MEMBER ZANZONICO: Pat Zanzonico. That was terrific. Really very thorough and clear presentation.

You know, now is not the time and place if there ever is a time and place to pursue linear non-threshold, et cetera, et cetera, that show a basis for a lot of these recommendations, but - and this is not a rhetorical question: Are you aware of any epidemiological studies which indicate that among NRC licensees, whether medical or non-medical, a statistically significant increase in cancer which mean compliant with the five rem limit?

In other words, is there any data other than the linear non-threshold theorizing, so forth, support dose reduction of any sort from the five rem limit.

DR. COOL: From an epidemiological standpoint, there have been several studies that have been done looking at various occupational databases.

Some of them have shown slight differences depending on data which is included or excluded.

In fact, right now there is underway - it's gotten nicknamed the million man study, to take the databases that are available in the United States in DOE, in NRC, and do a more detailed analysis on those looking particularly at the earlier years.

Now, we are fairly far removed where; one, doses were higher and; two, there has now been a fairly significant time period for a follow-up to see if there is anything that can be drawn from those studies. So, that information is not available now.

You have in addition to that, I'm sure you're aware, the ongoing work that the NRC contracted with a national academy to look at doses in populations round nuclear facilities and do a refresh of the study that was done in 1990 or so to look at whether there was any evidence of statistical differences for those populations at the very low environmental dose rates.

That is also in an ongoing process. The National Academy gave Phase 1 of its report with some recommendations for a pilot which the staff is currently considering.

There's the DOE low dose study program and other things looking at the cellular, molecular other

side of things and trying to work through the information. Low dose for them is 10 rem, but that work continues.

And you see a wide variation in things that are found depending upon single cells, small groups of cells or something which comes closer to tissue levels.

All of that information helps to contribute to our understanding. At this point, it does not provide information that would suggest that from a regulation development basis that we would have a basis to move away from a linear model.

Now, quite frankly, if I took off my NRC hat and said just Don Cool, do I think the radiobiological response of a human to radiation is linear? No. I don't know of any response that we have that's linear to anything.

On the other hand, I only know two reasonably effective regulatory structures. They're either lines, or they're a switch.

And so, within the construct of what we have while we certainly need to continue to look at what we know and refine that and apply what we know if we're looking at a particular case in point for the regulatory structure, I think we still need to be in a position of using this in order to have a consistent, predictable,

transparent process.

CHAIRMAN MALMUD: Thank you.

MEMBER ZANZONICO: Can I just make an editorial comment? Pat Zanzonico.

As much as I would like to say otherwise, because I just have this visceral suspicion - linear non-threshold model. I think given the available data and given the applicable risk assessment algorithms, it's really hard to argue against a reduction of either the occupational MPD to two rem per year, or in particular the lens dose MPD.

The one point I would make is, and I agree completely that certainly for medical work is the overwhelming majority, essentially a hundred percent, are less than two rem per year.

There is a practical and cost implication for reducing that dose limit nonetheless, because most sites use an action level of ten percent of the MPD. It's as reasonable as any in terms of triggering some reduction.

And so, by reducing the MPD from five rem to two rem, then obviously the action level for many sites will be reduced from 0.5 to 0.2 rem. And there may be practical and economic implications of that that are real, nonetheless, even though all of their workers are

below the two rem proposed limit.

DR. COOL: That's very correct. The question that Marge, although I didn't mention today, is a key question in terms of how you demonstrate compliance and your confidence that you will stay in compliance. I would agree.

CHAIRMAN MALMUD: Thank you. Dr. Van Decker.

MEMBER VAN DECKER: Thanks. A small handful of questions, if I could. Number one, help me understand where you are process-wise.

So, a SECY paper has gone and it says you want to continue where you're heading. And the ask to come back is continue to find a technical basis for rulemaking or what's going to come back is go ahead with rulemaking and establish stakeholders and your timeline for rulemaking.

DR. COOL: Thank you. I realized as you started to ask that, that I didn't actually tell you where we were.

The staff has given the paper to the Commission. The Commission is still in the voting process.

What the staff has requested is permission to continue to develop the regulatory basis over the next three years at least to the point in which technical

information like the dust coefficients would be available to have a regulatory basis upon which to write a rule.

Now, we have told them that we would like to go beyond what might typically be a regulatory basis development and actually look at the specifics of possible rule language in order to be able to check the implications. Normally, that's done after the basis is developed.

But in terms of process, this is a regulatory basis development, complete a regulatory basis roughly at the end of 2015.

With agreement to then work a proposed rule, there would be public comment on the proposed rule after Commission, there would have to be analysis, comments, agreement on the final rule, publication and an implementation period.

When you start to do the math on that, a possible effective date is 2020 or perhaps further.

MEMBER VAN DECKER: Okay. I understand the shrewdness of your answer. I like that very much, actually.

So, my second comment here is, you know, on an ALARA program basis, you know, most of the time raw data is being used to, you know, work internally and not

always, you know, effective dose is being calculated on all of this.

You need to recognize that internally we need to be doing something so that we're not chasing our tail on a large variety of things. And I'm not sure what can be done to help that out, but we'd have to think about it some.

And I guess my last comment on this is just the general comment, you know. There's nobody here that's going to say we're not against trying to provide the most safe and effective environment possible for occupational workers, as well as our patients and everything else.

And obviously, you know, the lower, you can go lower. It's always better than higher. And then the question comes, it comes at what cost and where does that cost go.

So, you know, what's in the purview of the practitioner or the occupational worker, which is obviously time, distance, shielding, right? But recognize that that pressure point which comes by this may not be the only pressure point that gets us as a society where we want to be.

Because as you pointed out, the majority of your five percent outliers are not the regulation within this room per se. It's mostly machine-produced, right?

Fluoroscopy, fluoroscopy, fluoroscopy.

DR. COOL: There is a substantial contribution out there, but I will also reflect that in our interactions with the states, one of the things that has been quite clear is that there can be only one set of requirements.

There are 37 agreement states. The adequacy and compatibility would apply. They will have a single set of standards.

MEMBER VAN DECKER: Yeah, okay. Well, we know I believe that. But my question and my comment is, obviously, you know, a pressure point on the machine on the production on what can be done technology-wise in addition to just the pressure point on the individual, obviously, so that there are really more stakeholders in this in a broader sense than just, you know, what you're there in and how they become a percentage of what can be done to help improve the environment rather than just the pressurization of time distance shielding.

So, and, you know, reference defaults on machine-produce may help, but some concept that this is a broader discussion needs to at least be recognized.

CHAIRMAN MALMUD: Thank you. Any other comments?

MEMBER LANGHORST: Dr. Cool.

CHAIRMAN MALMUD: Oh, Dr. Langhorst.

MEMBER LANGHORST: Dr. Cool, thank you. That was a very thorough talk on that, but you did not come back to other agencies and their implementation or evaluation of these dose limits.

And so, for agreement states I would understand that if they have to meet the NRC requirement, that they would apply that to all radiation sources, I would assume, but what is the - and you may not have answers, but what is OSHA doing in regard to their regulation on radiation control programs?

And another question I have is, would this impact the FDA's limit for human research subjects, which is currently five rem whole body or three rem to organs?

So, kind of a question for you, question for Dr. Suleiman, too.

DR. COOL: The U.S. interagency has this as an ongoing discussion. We have an Interagency Steering Committee on Radiation Standards that talks about it almost constantly.

The Environmental Protection Agency is looking at a number of things. And, in fact, has in preparations advance notice of proposed rulemaking to move - to propose or to discuss moving to this methodology in some of the general applicable environment standards

for the fuel cycle, 40 CFR 190, 192 and other parts.

On Monday will be the first formal meeting of an interagency subcommittee that will look at questions of whether there should be an update to the formal federal guidance on occupational exposure last revised in 1987.

OSHA put out a request for information some several years ago earlier on before we actually started this process, and is watching to see what we will do.

It's not active at this moment, but they are engaged in following the discussion and the process.

The Department of Energy completed just in the last year a couple of rulemaking, which moved the scientific information to the 1990 approach. They are also interacting with us, but at this point have not indicated an active consideration of any other changes to the system.

FDA is also represented on that committee, and we have two individuals from the states who are observers and actively participate in that discussion.

So, we're trying to keep tabs on it.

CHAIRMAN MALMUD: Thank you.

MEMBER LANGHORST: Thank you.

CHAIRMAN MALMUD: Dr. Suleiman.

MEMBER SULEIMAN: I have comments for you,

but I'll answer that question.

MEMBER LANGHORST: Thank you.

MEMBER SULEIMAN: The Radioactive Drug Research Committee writes those are independent. They apply to the research subject. So, right now they stand as they are.

MEMBER LANGHORST: Okay, thank you.

MEMBER SULEIMAN: I will share with you that we've been wanting - I've been wanting to readjust those, you know, because I think research is risk based unlike occupational protection, I mean, the way the standards - standards are protected, you know, you have like a 55 mile an hour speed limit so all of society is safe You don't have a speed limit for each car and each person or whatever. But with research, you've got people with different ages and whatever. I mean, I'm just sharing with you what's going through some of our minds.

The questions to you, Don, or at least just to let you know what I think, my observation is that ALARA more so is appropriate, it seems to be working in occupational.

I think in medicine it's not - and probably that's not relevant here, but it's not practice. People don't often even know the doses they are giving.

So, I always argue that the first step in

practicing ALARA is knowing what you have in the first place. So, how can you make sure you're reducing the doses if you don't know what you have?

A little anecdotal story that I think is important in sharing, we had a poster to be presented in some meetings a couple of years ago on RDRC. And we had the RDRC limits and other dose numbers up there from a variety of radiation sources, including background.

And I found it really, really interesting to me that some of our - we have a lot of smart, educated people at the agency. Obviously a lot of them don't have radiation background, but they picked up on the general population limit of one millisievert and similarly with you were talking about the fetal limit, and they said, why would you have a limit that's less than background radiation? Because we had the background level there.

Can I just share that with you? I think - I also feel that if the two millisievert limit is attainable because you've got data that shows that and I've heard from colleagues in New York who say people seem to be complying with it.

But as long as we at some point we say this is fine, we can't keep - just because we can detect lower, we don't want to keep on lowering things where it becomes impractical, but I share that one millisievert

observation both regarding the limit to the fetus and to the general population.

So, I'm comfortable with what's being proposed. I just wouldn't want to get ridiculously lower here.

CHAIRMAN MALMUD: Thank you. Other comments or questions? Dr. Welsh.

MEMBER WELSH: Jim Welsh. Appreciate the presentation and the perspectives, but I have to say that I, as an individual, am not in favor of lowering the dose limits. And I would call your attention to the ASTRO paper that was submitted to the NRC in January 2011 addressing this issue in which that organization also posed reduction in annual limits.

And I would ask if stakeholder representation has been provided by ASTRO, AAPM, ACR and the other really large players which have a large population of radiation biologists to provide input to perhaps balance the perspective of the ICRP, the NCRP and their reports.

Because as we all know, there are extremely differing opinions on this subject and I, for one, do not feel that the ICRP report accurately reflects the reality.

So, I just ask if AAPM, ACR, ASTRO has

continued to weigh in as we proceed and make these recommendations.

DR. COOL: I believe all of those societies were present seats at the table in Los Angeles. I'm not sure that all of them actually formally submitted comments on the work group.

Our intention if the Commission agrees that we should continue this dialog and start to look at specifics and details, is that we would be both welcoming and trying very hard to get all of those players to the table and interacting to try and have the best understanding of the various implications.

CHAIRMAN MALMUD: Thank you.

DR. COOL: Thank you, sir.

CHAIRMAN MALMUD: We'll move on to the next presentation. Mr. Mattmuller.

DR. COOL: Before we do, can I make a request that I can also join the subcommittee on the AO events?

CHAIRMAN MALMUD: The subcommittee we just formed, absolutely.

DR. COOL: Thank you.

CHAIRMAN MALMUD: You are hereby appointed, unless the chair objects.

MEMBER LANGHORST: Not at all.

(Pause in the proceedings.)

MEMBER MATTMULLER: Good morning. I'll give you an update on where we are with molybdenum-99, an update on the progress we're trying to make for a safe, robust and affordable supply of moly-99. And or course it's very important to us because that's the parent to technetium-99m, the most commonly used nuclear medicine diagnostic radionuclide.

And for the test of my talk instead of stumbling over molybdenum-99 each time, I'll refer to it as moly, and technetium-99 as technetium.

And technetium is used in about 80 percent of all procedures and worldwide. And the majority of the moly used with technetium comes from highly-enriched uranium which is defined as greater than 20 percent. But typically the targets that are used for moly production are around 95 percent.

And, unfortunately, there are countries in the world that have a strong desire for HEU and are interested in its use for, shall we say, non-constructive uses.

And so, there's a coordinated multi-national effort to - sorry - to phase out the use of HEU in the world, but our need for moly right now for our technetium is about 12,068 curies per week, which is somewhat of a bizarre unit.

But that's defined as a unit of measure for moly producers present in a shipment six days after it leaves the producer's facility. And in the US alone, we use up about half of the world's need for moly-99.

So, let's take a look at our supply chain and why it's often characterized as being fragile. On the left we have the reactors around the world. None are in the US. And some have multiple supply lines to the producers in the middle. And then to the far right are the two US generator manufacturers.

All these reactors currently right now are using HEU for moly production, except the two exceptions here at the bottom, or at least OPALs at the bottom. that's the Australian reactor. And they're 100 percent LEU. And the SAFARI reactor in the yellow is about - they're in the progress of changing over and they're about 50/50 right now. They use LEU to HEU for targets.

Complicating this supply line are the large distances between reactors to producers, to generator manufacturers. International borders have to be crossed.

You're talking about radioactive packages that are in Type B packages as opposed to the Type A that we're most familiar with which can be a robust cardboard box. Type B is usually a steel and concrete-type structure that has to also withstand accidents. So, it's

a substantial, expensive and difficult package.

One of the other bigger concerns for our fragile supply is the age of the reactors. Most of these you could say are baby boomer reactors. They were commissioned in the `50s and `60s.

Two exceptions. The Maria, you could say, is a Generation Y in that it was rebuilt in 1993. And the newest is Generation Z, the OPAL reactor down in Australia, but unfortunately for us it's halfway around the world.

So, as some - and also contributing to this issue is some reactors supply more than one producer. As you can see the lines crossing from reactors to different producers.

But even in this process of converting to LEU, the producers can be a bottleneck in that not just do they have to redesign LEU targets that work in the reactors, the producers now have to redesign their processes to handle the LEU targets and which usually means they need more hot cells, which are very expensive. And they have to deal with more waste than what they typically use or typically are accustomed to.

And as an example, well, it used to be an example, is the OPAL reactor. The OPAL reactor can actually produce a lot more moly than it does right now.

And my talk is now out of date as of two days ago.

They didn't have the processing capability to handle the additional moly. But if you're a real moly junky, you may have seen the new story that came out two days ago where the Australians are going to invest about $170 million into a new processing line so they can, in essence, double their production capabilities of moly to the world, which is great news. I just wish they were a little bit closer to us.

So, that's probably the best news we've had in a real long with regards to moly, and that just came out two days ago.

This is also a partial diagram of the supply chain which missing to the right of the manufacturers are the hundreds of nuclear pharmacies around the country that take the technetium generators and prepared the technetium kits and then send out to the thousands of nuclear medicine departments around the country.

And this is all with the clock ticking with moly with that half life of two and a half days and technetium with six hours.

So, it's why we always say this is fragile, because it's a time sensitive product, complex in distant supply chain, reactors near the end of their lifetime, the need to convert to LEU and also the need for

processors to convert their systems to LEU.

Here's an older slide from 2010 of where moly comes from. It doesn't have the contributions of the newer reactors that have been added lately such as the Maria reactor in Poland or the LVR15 in the Czech Republic, but - and their contributions are important, but that's still a relatively small percentage, but still the big five on this diagram are responsible for 95 percent of the moly.

The NRU being the oldest in Canada, and unfortunately whose breakdowns over the years have sort of made it our poster child for our fragile moly supply. And it's scheduled to be shut down in four years in 2016. It's handling 31 percent of our supply right now.

In 2016 when the NRU shuts down, this is what - well, somewhat our slide is going to look like, because hopefully by then the Australians will be into this.

But in Canada, they have no plans to update the - to replace the NRU. In Canada, they have a two-prong program for producing moly or technetium for just Canada. They're going to have a network of cyclotrons to produce technetium directly and to distribute it quickly, of course, within metropolitan areas.

And then they also have a second program where they're going to use linear accelerators to produce

moly versus a gamma neutron reaction on stable moly-100 much in the same way as NorthStar here in the US plants produce moly. And I'll be talking about them later.

Also in the news recently has been the Maple reactors. There is some legal wrangling going on between AECL - or what's going to operate the Maples versus Nordion, but I think it's just a business legal dispute of course involving money.

Because if you look at the Maples, they were originally designed for HEU fuel and HEU targets long before the moly issues came to light.

And they're having trouble - well, they can't get it to operate properly now as it was originally designed. To get it to operate with LEU targets and LEU fuel would practically require redesigning the whole reactor from the ground up.

So, I think personally it's very, very unlikely that we'll ever - they'll ever be recommissioned. I think, unfortunately, especially in terms of moly, we'll never receive any from the Maples.

So, there are plans, fortunately, to update some of the big five reactors around the world. The first one I'll talk about is the BR2 in Belgium. And this is a design for the replacement reactor, the MYRRHA. And it's actually going to be more of a two-in-one facility.

Their plans for it are to be called Europe's fast spectrum irradiation research facility with a secondary aspect for radionuclide production.

And they do plan to use LEU fuel and targets for this. This is some of the different reactors though that you may have seen and that there's a standard research reactor to the right, but also they are going to have an accelerator produce protons directed into the targets within the reactor so they can have, I mean, usually test reactors just irradiate neutrons. This one will be able to irradiate with neutrons and protons. So, quite the hybrid.

Their plan is to have this operational in about 11 years. So, it's still some time away and they've not even started to dig for it yet.

The next one would be the HFR in the Netherlands. The replacement is called PALLAS. And they, too, plan to use LEU fuel and targets for the new reactor. And I should back up a little bit in that one of the efforts currently going on right now is Covidien. It's working to develop LEU targets that would work in both reactors on both the BR2 and the HFR right now, which is somewhat a bit of a challenge to get one target to fit and work in both reactors.

So, Covidien is actively working on that now

as part of this process to phase out HEU now rather than later. But certainly when these new reactors come online, that will also take care of the issue in that both fuel and targets use LEU.

This one also in on what I would call a slow timeline. It's about 11 years away before they commission it.

Here's one I can get excited about. From the donut, the OSIRIS French reactor is going to be replaced with the Jules Horowitz reactor. And this is a national image from about a year ago of their construction site.

So, its plans are approved, construction is underway, they're making great progress and their hope is to have this operational in about three years.

But some like the Belgium reactor, the problem with this reactor is that it's really designed only for irradiation testing. They weren't really interested in radionuclide production. So, now it's sort of being added as an afterthought and here's a diagram of their reactor core and test pools and such in that now they figure they can squeeze in moly targets that would maybe be 500 targets a year.

They think it can maybe squeeze in a thousand targets a year. But if they put in a thousand, then it starts competing with other targets that they had

originally planned the reactor for. So, it's not an automatic.

500 targets a year they estimate would produce about 2,000 six-day curies per week. So, about one-sixth of what we need in the world.

So, back to our donut of moly. If we add in the French reactor in three years, their old reactor is eight percent on the right, the new one gets to 25 percent of the world's supply is 17 percent. Some crude drawing skills, and this is what our moly looks like. Still missing 14 percent.

At this point, it's too soon to know how soon the Australians will be up and working, but I'd like to think they'd be up and operating far sooner than the other reactors who are a good 11 years away.

So, we still have a need for more moly especially here in the US. And hopefully it will come from one of the four projects that currently are underway here in the states that are through the Global Threat Reduction Initiative. That's Department of Energy's national - or security agency or administration, but they're GTRI to get civilian - to reduce civilian use of HEU and replace it with LEU where possible.

The GTRI program is providing technical support for these groups through Los Alamos, Argonne

National Laboratories. And they're also providing multi-million dollar grants. And they're also, you know, to date moly production has been in a lot of reactors that have other functions and other support from the governments and there's really not been a true commercial market model for moly.

Well, the GTRI is now saying you have to do it with LEU and you have to have full cost recovery. So, it's like get rid of all the fuzzy economics that exist today.

And the big issue with that is waste management especially here in the US since there is - well, the waste is an issue. I won't comment any further.

So, the first of these projects is with GE. And they were going to redo an old process of neutron activation of the moly-98 cold nuclide to produce moly-99. And this is the way moly used to be produced years ago before fission took over in popularity.

The biggest issue with this is that moly produced in this method typically is two to four orders of magnitude less than a fission moly that we produce now. And the problem is, is that then you need to use a bigger column in your generator.

The column for an approximate comparison for a fission moly used in the generator today, is about

the size of a piece of chalk from - hopefully you all remember what a chalkboard looks like - versus a column for neutron capture moly is maybe about nine, ten inches tall and about the thickness of a broom handle.

So, a much bigger column which produces - which the biggest issue was that it limited the amount of moly that you put on the column. So, the generator should not nearly be as big as what we're accustomed to today.

So, GE was trying to address this issue by looking at a technology called gel generator technology that I believe in India they are using, but they've only been - in India, they're only successful with it with very small generators. I don't even think they exceeded one curie in size. So, completely ineffective for our uses.

And so, sadly at this point in time, GE has put their program on hold. So, they're no longer an active participant.

Another group that's looking is Morgridge Institute of Research. And they've partnered with a group called SHINE Medical Technologies. And they too have gotten awards from - through the GTRI program, but they're working on a brand new program - or process, I should say, for producing moly.

And instead of using neutrons from a

reactor, they're trying to use a process of using neutrons that are made from the reactions of two different isotopes of hydrogen, of deuterium, or heavy hydrogen, and tritium.

And so, in their proposed accelerator, they'll be pushing ions towards the target chamber - or the deuteron ions, excuse me, the gas flow is accelerated. And the accelerating deuterons strike the tritium gas in the target chamber creating neutrons.

And then the neutrons are multiplied by the beryllium multiplier. And then these neutrons strike in the blue segment there, the aqueous LEU target. So, it starts a subcritical fission of the LEU uranium to produce moly.

Their projected production rate for a single unit like this that's about six feet tall, would be about 500 six-day curies per week.

It is an interesting new process because it doesn't involve a research reactor. However, one of their big challenges will be dealing with the waste, because they still have fission of LEU uranium.

A third company is Babcock & Wilcox and they too are pursuing a different technology using what they call a MIPS or a modular isotope production system, where the fuel and the targets are one in the same liquid and

fission occurs.

And then at some point in time when they feel there's enough moly has built up in the fission process, they remove the solution, separate out the moly.

And of course whenever there's fission of uranium like this with either process, neither process, most processes, only a small percentage can actually fission occurs to produce moly.

So, there's substantial cost savings to putting the solution back into the reactor to let it continue to build up its moly production.

They've been at this probably the longest of the groups. And as they put it, they have completed Phase 1 which included conceptual design, bioengineering. They've completed research projects with Argonne, Los Alamos, Purdue University. They've got their QA plan in place with the NRC, but then the other challenge is market conditions.

And so, actually, they've put their project on hold right now, too. They are not going further yet. So, unfortunately, it too is on hold.

So, the fourth group in the US is NorthStar. And they too are proposing a nontraditional method for moly production.

Like the Canadians, they are using a

high-power electron beam generated by a linear accelerator. The beam strikes a solid tungsten window and this creates a bremsstrahlung radiation or breaking radiation.

And for a quick Physics lesson, bremsstrahlung radiation is electromagnetic radiation produced by deceleration of an electron and deflected by another charged particle. Typically an electron.

The electron uses its kinetic energy and it's converted into a photon because as all the physicists will tell you here in this room, energy is conservative.

So, and this reaction has a big - again, we're starting - the GE reaction, we're starting with a cold, stable moly-100 in this case. And the photon interacting with the nucleus causes the ejection of the neutron and it's converted to moly-99.

So, a huge upside to this process is that there's no fission of LEU. There's no uranium, plutonium or fission waste that they have to deal with.

The one downside they do have similar to the GE process, is that it will be low-specific activity. So, that is the challenge, but then they're also working on new technology that I'll explain later to address that issue.

So, I hitchhiked up to Argonne to see their linear accelerator that they're using for their test. And the accelerator they have there, they're using - the beam is - actually from the diagram on the left, the accelerator sits about where it says "Argonne." And the first unit you see is actually the beam splitter.

And part of the beam goes to the alpha magnet, which in the photograph above it is the green magnet structure or what I would call a U-turn magnet, but I'm not a physicist. So, then this from one beam, they're able to split it and irradiate the target on both sides. Also in the inset, there's a smaller beam magnet about - like bends at about ten degrees.

They have completed some tests on their targets, but right now they're in the process of upgrading the energy of their linear accelerator so they can perform higher energy tests.

Now, they're also still moving forward for their production plans and they're going to be building a plant in Beloit, Wisconsin with about 12 or 14 sets of linear accelerators.

And in the production plant, they'll have two linear accelerators on each side of the target using - they won't be directly aligned with each other. They'll be offset with using a magnet very similar to the red

10-degree bending magnet.

To me, personally, once they're fully operational for the number of linear accelerators they're going to be using, they're going to use the electricity equivalent not to one, but three auto assembly plants.

So, instead of having three large auto assembly plants, there's just going to be this one plant drawing the same amount of electricity. That's a lot of electrons.

So, the target in moly production, this is the actual target that they're using up at Argonne. In the inset, this is a blown up image of the target holder that has 25 slots in it. Currently they're using little wafers - not wafers, but slugs for an inelegant description, that's about a millimeter to 12 millimeters in diameter. It's about the size of a dime of the moly-100.

Now, if you've got two high-energy electron beams on you, you're going to get warmed up. So, to remove the heat from this, they're using helium gas to recirculate through the target. And that's why you can see the two big ports on either side. That's for the helium and flow of cooling system.

For their actual production linear

accelerator system, they are planning on using a bigger version of this target where the disc of moly will actually be about 25 millimeters in diameter or about a little bit bigger than a quarter.

So, no more physics, but hopefully you're up for a little bit of chemistry here. As I've mentioned before with the GE process and with the NorthStar process, it's low-specific activity moly.

So, for a conventional generator system, low conventional - or excuse me - low-specific activity moly would require the larger column reducing the amount of moly they could put on it. So, how to solve this problem.

One way is the brand new generator technology that involves what they call ABEC chromatography, which is aqueous biphasic extraction chromatography.

In this system, the first generator column is an ABEC column. Or a little bit less of a mouthful would be a primary separating column, or PSC is how we refer to it.

The PSC is a polymer, a polyethylene glycol, which is the static chain to the right on a base molecule of polystyrene divinylbenzene. Like I said, the PSC.

And it's suitable for a two-phase system of

separating out liquid, separation of metal ions such as moly and technetium.

And the first big difference with this type of generator system is that the current generator is the moly on a solid phase aluminum column. In this generator system, the moly is going to be in a liquid solution adjacent to the generator.

The first step then would be to pass the moly technetium mixture through the PSC column where the moly has very little affinity for it, but great affinity for the technetium. So, the technetium is going to be extracted and adhere to the PSC while the moly passes through and goes back to the vial.

So, this has an advantage in that since the moly is all off or out of the mixture, you just have technetium on your column. You can then pass saline through your PSC to cool off your technetium.

And regardless of your low-specific activity moly that you started with, you can get high-specific activity technetium in your collection now which is great for nuclear pharmacies for producing kits as they do now.

So, this is a little bit better schematic how the generator will operate. As I said before, the big difference is the moly and the technetium in a mixture

in a solution in a vial separate from the generator.

It's pushed through the ABEC PSC column, and this actually shows it going to a separate vial. But in essence, the moly would continue back to the original solution vial.

the technetium is then alluded off of the ABEC by saline running through the ABEC through the aluminum guard column. And this is an additional purification step just in case there is any additional - or I shouldn't say additional, I should say residual moly that's on the PSC. It will be trapped by the aluminum on the guard column so to ensure that our final product of technetium is equivalent to what we get now.

If you split this diagram in half, you basically have a diagram for the technetium generator that we have now where the moly is on the aluminum column already and we just pass saline through it to pull off the technetium.

the other advantage for this system is that once the moly-99 has decayed away, the residual solution can actually be returned to NorthStar and they plan to recover the residual moly-100 that's in the solution that was never irradiated.

So, there is of course an expense to having moly-100. So, they're able - part of their economic

market plan is dependent on recycling the unused moly-100.

So, this is the current plan they have - or I shouldn't say - version of what they call their TechneGen generator. And this is up at Argonne right now.

In it, you can see the two - but at the bottom there at the vertical, those are two syringes that are used for pulling and moving the solutions from the different vials through the different columns.

Above them are multi-valve systems with different lines going to the vials or the reagent vials that are on top.

To the left you can see a stainless steel and a lead-shielded vial. The one would be for the moly-100 - or excuse me - the moly-99/technetium-99m mixture. The other one is a waste vial.

The PSC column would sit - you can see the four vials on top and there's a square lid there. That's where the PSC column actually fits in this unit.

Different solutions fit on top, and the technetium collection vial, shielded collection vial, would fit on the far right of this unit.

This is - they've gotten to the point where they are - actually, they've been active in talking to the FDA and they're actually very close to submitting

this to the FDA. So, they do have a prototype what they call their moly-technetium reagent kit, which is good for five elutions using this system.

In it is the primary separation column which is difficult to see in the bottom right and a clear plastic back. Behind that are the four different reagents that will be used for the elutions.

Actually, one of the vials has hydrogen peroxide in it that they'll use to clean and sanitize the pathway of the tubing from the PSC to the collection vial.

There's a sodium hydroxide in it, which is the solution used to move the moly-technetium mixture through the PSC to the waste vial.

There's also - I forgot to mention this earlier. There's also a vial of sodium acetate that once the moly-technetium mixture has gone through the PSC once, they use sodium acetate to run through it also again as a purification step to pick up any residual moly that's still on the PSC before they elude it to the guard column.

Also in this picture on the bottom left you see blue that are small filters, adapters that in this current kit attach to the vials before they put it on top of the TechneGen. And all this right here is good for five allusions.

The next part to this process is the

technetium collection kit. And this is what they have with their current version.

You have the guard column which is, sadly, difficult to see to the left. In the middle is a new - is a needle that they've worked on. It's actually a two-in-one needle in that one puncture of the septum as a port for flow of the technetium into it. And the other port is used for venting the vial so there's equalization of pressure and it flows easily.

The collection vial you see, and also from a nuclear pharmacy perspective our old friend the blue millipore sterilizing filter with a 0.22 pore. And this is actually the same type of filter that's used in current generators right now and its flow pathway.

So, this is assembling the collection kit here and it's also showing the two-part lead shielding that's used.

The collection vial of course goes in the bottom half on the right. What the picture in the inset is trying to show is this two-part needed. It's there if you strain. I could have used a bigger, better picture, but someone on the staff made a complaint about that, but we won't go there.

What you can see just above the inset is the guard column, the blue millipore filter, the dual

two-in-one needle adapter all assembled. And then there's a core plastic shield that goes over that.

That whole assembly then goes in the top half of the lead shield that then is put together on the bottom half holding the collection vial. And there's little notches that fit into - or tabs that fit into notches to lock it together securely.

This is then put on the right side of the generator. So, you have - it's all set up. Your PSC's in place, your vials, your solutions are in place, the collection vial is there.

Then to lift the generator, you hit "Start" on a computer. And the computer controls the vials, the movement of the liquids through the different vials through columns and whatnot. It's a completely automatic process.

So, to borrow a line from - ad line from Oldsmobile, this is not your father's generator. So, completely different.

You can almost think of this more as a hybrid between what we have for a standard technetium generator now and what we use in PET for F18 and FDG synthesis with the chemical synthesis unit. And likewise with the PET module we add our reagents to it, put our vials, our sterilizing filter in place. Close up the box between the

hot cell and then hit Start on the computer.

So, there's been a couple different variations in the FDG modules. More of a second generation module. It would be set up similar to this to where you have individual vials of solutions.

Current generations of FDG synthesis modules now have a cassette where each individual vial is already fixed in place into this plastic cassette that can only go in one way into the module.

And so, that's a nice difference in that you can imagine at 0 dark hundred in the middle of the night a pharmacist trying to set this up where he might get the vials in the wrong order. If you have this cassette, then it eliminates that possibility.

So, and NorthStar is now working on that cassette system. So, they plan to have that with our next generation.

So, they have already done some testing with this generation of TechneGen. And they've already tested up solutions up to two curies of moly. And the technetium elutions have passed all QC tests in regards to sterility, pH, moly breakthrough.

And then they've also taken these elutions and they've prepared technetium kits with them. And quality control in the kits has also passed all quality

control tests. So, it's a system that's working very, very well.

So, this represents Part 2 of their plan. Part 1, of course, is the production of moly. With their process will be a problem with standard generator. But this new technology, it's a very elegant solution.

In fact, they plan to go to market using moly produced by the MURR reactor in Missouri using the same process that GE was going to use. That is the neutron bombardment of moly-98 to produce moly-99.

So, they're not waiting for their Beloit, Wisconsin facility to be constructed. They're planning then to market, sooner rather than later, using moly from Missouri.

And then once their production facility is up and running, they then plan to use just the moly from Wisconsin.

Now, the other interesting thing about this generator is that conceptually it can be used for other separations of different parent-daughter radionuclides.

And they've already tested it for separating the alpha emitter bismuth-213 from its parent actinium-225. And it's also been used for separating gallium-68 from its parent of germanium-68.

So, the ABEC chemistry has other

applications besides technetium and moly that we may see in the future.

So, we're making slow progress on new reactors and new LEU targets. We do have some very promising US producers for moly. And we have exciting generator technology on the horizon and soon a new source of moly from the MURR reactor here in Missouri using end gamma reaction stable moly-98, but so far we still don't have a solid and fair - fair plan yet and just how to pay for all this.

Perhaps the biggest challenge in this whole process will be obtaining adequate reimbursement, which is of course likely to be for much more expensive moly in the future.

So, metaphorically I would say we're between the rock of the GTRI saying no more cheap HEU fission moly for our field, and the hard place of limited additional reimbursement from CMS for more expensive moly. Thank you.

CHAIRMAN MALMUD: Thank you, Mr. Mattmuller. Oh, I see we have some questions. Dr. Welsh.

MEMBER WELSH: Yes, thank you. Thank you, Steve, for that wonderful presentation. And I can't help but believe that it's not by accident that you omitted one of the major players in this whole arena.

And just in the way of disclosure and fairness, you all know I've been on this committee for about six years and I've given presentations very similar to what Steve has just given.

And I think it was Dr. Malmud who said at the conclusion of my presentation that it looks like I'm calling for a very large Manhattan Project scale US effort. And I was, but I've grown tired of holding my breath waiting for that to happen.

So, I am on the board of directors for a company that does plan to make moly in the United States. And the name is Co-Key, in the way of disclosure.

Just in way of information, this is - the plan is for twin 20 megawatt research reactors to be housed in Gainesville, Florida using in-depth designed LEU fuel, LEU targets just like the OPAL reactor of ANSTO. The projected output is 7,000 six-day curies per week, 365 days a year, which is very favorable compared to anything else that's been proposed.

And also unlike some of the other innovative technologies mentioned such as neutron capture and photonuclear reactors, this technology makes moly-99 and the therapeutic isotopes that are important to me as a radiation oncologist.

Also, unlike some of the other innovative

concepts with low-specific activity moly, this approach uses an FDA-approved extraction method for its moly which is identical to the Australian OPAL reactor.

There was a presentation to the NRC on June 8th of this year. The environmental report gets submitted in December of this year. So, just a little addition to Steve's otherwise excellent and thorough presentation.

CHAIRMAN MALMUD: Thank you, Dr. Welsh. Dr. Van Decker, I believe, was next.

MEMBER VAN DECKER: Well, first of all, I want to thank both my colleagues. I thought it was great scientific discussions and it's good to see activities going on, because I think everyone in the clinical realm is worried about the age of the reactors we're working with and the HEU, LEU mandate. And so, you know, concerns about, you know, what's available in the future.

I guess my question to both of you, and it has to do with something else going on in parallel, is, "Where do you see the cost of technetium rising to percentage-wise to where it currently is given any of these methodologies and the hoops and the hassles and the push buttons and - because access, I mean, access to the patient is obviously the bottom line of this, right? So, ballpark?"

MEMBER MATTMULLER: Ballpark, easily double

the cost of moly is what I've read and seen, but that's for moly.

And so, in a good, efficient nuclear pharmacy for every atom of moly or every millicurie of moly, you can get five millicuries of technetium out in a dose.

So, if there's a hundred percent increase in moly, then there's a 20 percent increase in technetium to the patient.

So, and this gets to be very contentious in different economic models of the different groups. There is the OECD, which is a European group mostly the US is participating in. And they're looking at it and they're just starting - or have just started a more in-depth analysis of trying to get a better handle on this.

It's hard to get good data from the different manufacturers, different reactors. Some of this is market sensitive data that they don't like sharing. Some of the reactors get different levels of government support. So, it's hard to figure out what it really costs to make the moly.

Some of these reactors have other functions as far as test facilities that generate income in that regard as opposed to a reactor dedicated just to moly

production.

MEMBER VAN DECKER: So, the business model concern of this is obviously you well alluded to, you know, the CMS draft rule starting January 1st has put into place a tiny incentive -

MEMBER MATTMULLER: Yes.

MEMBER VAN DECKER: - to the end producer.

MEMBER MATTMULLER: Yes.

MEMBER VAN DECKER: A tiny incentive to the end user -

MEMBER MATTMULLER: Yes.

MEMBER VAN DECKER: - to purchase LEU-produced moly.

MEMBER MATTMULLER: Right.

MEMBER VAN DECKER: Buy a new coding system and add on the administrative cost in order to incentivize the use of LEU from overseas rather than HEU.

MEMBER MATTMULLER: Right.

MEMBER VAN DECKER: The odds of that going up the supply chain to all the people you just put there to really making LEU-produced moly easily available -

MEMBER MATTMULLER: Right.

MEMBER VAN DECKER: - is, unfortunately, unlikely to be the case by any stretch of the imagination although it's kind of an interesting concept. And

obviously it is an investment of money that's going up the chain and then going overseas.

So, you know, the concept of having an investment at home that pushes science and technology and may have other pieces to it, obviously, is attractive so long as, obviously, the cost containment - and the healthcare cost containment era also is a piece of the puzzle.

MEMBER MATTMULLER: That's a great summary as to why I put "fair," because - into my last statement about fair reimbursement. Because what CMS is proposing in a perfect world would work if everyone switch from LEU to HEU moly at once and everything was then HEU, but this is a gradual phase-in process for drop of HEU, increase of LEU.

And so, how does a producer keep track of this moly came from HEU, this came from LEU, this is eligible for the additional payment, and then the generator manufacturer has to keep track of it, and these reactors don't operate every day of the week throughout the year, you know, they have to shut down for maintenance and such.

So, the pharmacy could have a generator with LEU-produced moly in it this week. The same generator next week would be HEU. So, then how do you keep track

of that with your different customers and they keep track of it to say, okay, I can charge $10 more for this.

It's very, very cumbersome and complicated and impractical.

CHAIRMAN MALMUD: Dr. Suleiman.

MEMBER SULEIMAN: Nice presentation. I've been involved with the OECD group and typical technetium, it depends on the drug, which costs differently, run around four to $700 for the entire procedure.

The cost of the technetium-99 component depending on the size of generator you buy, whatever, has been estimated to be in the several dollar range.

When CMS made the decision to go with a $10 - July 6th they proposed in a Federal Register document to reimburse preferentially an additional $10 for LEU-manufactured technetium-99. And the intent of that was to stimulate, because you now have all the molybdenum coming from Australia and from - South Africa also sends a pure LEU-based moly. It's not all being sold.

Because right now even though at some point the NRU, the Canadian reactor is going to go offline, they are online right now and they're producing a significant amount of HEU-produced moly. So, you have a financial disparity.

So, the intention was to sort of stimulate

and get people to start buying the LEU-produced moly-99 and give them a $10 out of a $700 - one of the companies has actually stated that they will be producing 100 percent LEU-based moly effective next year.

And the other question is, will there be people who are willing to buy? You know, is that, or isn't it? I mean, I've raised the question where I've heard the critics and I said, it's just an experiment. If there are no takers, then it will fail.

This is just intended to make the transition smoother. CMS shouldn't have bothered with the $10 simulation and wait for the reactor in 2016 to shut down. The transition will happen. It will just be much more bumpy.

So, I think CMS over and above their usual work, you know, made an effort to try to help stimulate this transfer. So, that's the intent there.

The comment was published July 6th. So, I guess they'll come out - they do this annually. So, you talk about getting rulemaking. It's always fascinating for the regulatory agencies, but every year they apparently do this to set the prices for Medicare reimbursement on an annual basis.

So, they say this is what we're going to pay for next year, and we publish it and they allow people

to comment for 60 days. And they do this every, you know, every year. So, I assume there will be some sort of final decision on this.

But right now there's actually a large supply of molybdenum out there. And the firms that have invested in the LEU production were sort of saying, we're there, but there aren't any buyers.

Now, clearly that will shift dramatically in 2016. So, I think things are moving in the right direction, but the cost, the technetium component of the total procedure, including the drug, is extremely, extremely small, you know.

CHAIRMAN MALMUD: I think the encouraging news is that there are many different groups working on this. And, therefore, the marketplace will dictate which are or which one is successful.

Hopefully it will be more than one successful one and try and keep the cost as low as possible in the open marketplace.

So, it's encouraging because only last year there was gloom and doom with regard to the supply of moly for the production of technetium, and now it's much more optimistic. So, we thank you for a very thorough presentation and I think we're all encouraged by it.

If we may, we'll move on to the next item

on the agenda, which is NRC staff. And I think - is Sophie Holiday going to do the work? Yes, Ms. Holiday.

MS. HOLIDAY: Hello, everyone. All right. This is our favorite part where we pull out our calendars. We're going to pick our tentative dates for the spring 2013 meeting.

As you may recall, I sent out a Meeting Wizard scheduler where everybody gave feedback for their possible open dates.

One thing I want to mention before I give these dates is the Committee has brought up that they would like to meet with the Commission. I have tentative dates that are possible for us to meet with the Commission, and then I have a separate set of dates where if you would like to plan it without having a Commission meeting.

CHAIRMAN MALMUD: What are the possible dates for the Commission?

MS. HOLIDAY: Okay. The number one choice for a possible Commission meeting would be April 22nd and April 23rd. That would be a Monday and a Tuesday.

CHAIRMAN MALMUD: Well, what about choosing that one preferably if we can get a group together since that would be able to reduce the number of travels.

MS. HOLIDAY: Okay.

CHAIRMAN MALMUD: How about the 22nd and 23rd?

MS. HOLIDAY: Okay.

CHAIRMAN MALMUD: Is anyone not available the 22nd and 23rd of April?

MEMBER PALESTRO: I'm not.

CHAIRMAN MALMUD: Chris, you're not.

MEMBER PALESTRO: No, I'm not.

CHAIRMAN MALMUD: How about April 15th and 16th?

MS. HOLIDAY: The only other date that would be available for the Commission would be May 13th and May 14th.

CHAIRMAN MALMUD: May 13 and 14?

MS. HOLIDAY: Yes, and that's another Monday and Tuesday.

CHAIRMAN MALMUD: May 13, 14, anyone not available then?

MEMBER PALESTRO: Me again.

CHAIRMAN MALMUD: Well, if that's not possible, then we would have to have a small group come down and meet with the commissioners on a separate day.

So, it looks like April is shot if Dr. Palestro can't make the 13th and 14th. There are no other two other days available that don't conflict with the

National meeting.

So, let's go back to March.

MS. HOLIDAY: So, if we were to consider days where we know the Commission is not available, it seems like the best date for everybody where I did not see conflict was April 15th and 16th. That's also another Monday and Tuesday.

CHAIRMAN MALMUD: Is everyone available April 15th and 16th?

MEMBER MATTMULLER: Can we bring our tax accountants with us?

(Laughter.)

CHAIRMAN MALMUD: April 15th, 16th sold.

MS. HOLIDAY: Okay. So, I'll put that as our first choice.

Now, we actually have a couple of choices as our backup dates. I have Thursday, April 18th, and Friday, April 19th.

CHAIRMAN MALMUD: Is everyone available for that date?

MEMBER PALESTRO: That's the ABS meeting.

MS. HOLIDAY: ABS?

CHAIRMAN MALMUD: 18th and 19th, so that's out.

How about April 22, 23? Not available, all

right.

April 29, 30 as the backup date.

MS. HOLIDAY: Dr. Palestro, are you available at that date?

MEMBER PALESTRO: Yes.

MS. HOLIDAY: Okay.

CHAIRMAN MALMUD: Looks like we have no indication of unavailability on that date. So, that could be our backup, 29, 30.

MS. HOLIDAY: Okay. So, then I have our first choice is April 15th and 16th, and our backup date would be April 29th and 30th.

And then, if it helps, then we could arrange a separate meeting with the Commission with a smaller group.

CHAIRMAN MALMUD: Yes.

MS. HOLIDAY: Do we have a problem with meeting those dates or those proposed - no, okay. And, actually, I have a handout to pass out.

(Pause in the proceedings.)

MS. HOLIDAY: Just one sheet. This is the portion where we go over our recommendations and our action items that were brought forth during these two days.

(Pause in the proceedings.)

MS. HOLIDAY: Okay. Item Number 6, Dr. Malmud asked NRC staff to find data on events in which the radiopharmacy has dispensed the incorrect amount of a radiopharmaceutical. That is an NRC action item.

Are there any questions, comments or concerns with that item?

MEMBER WEIL: Did we ask for a broader range of incorrect administrations or dispensing? Was it just incorrect amount? Was it incorrect isotope? I mean, it was a request for error.

CHAIRMAN MALMUD: Yes, the issue was the usefulness of the dose calibrators.

MEMBER WEIL: Right.

CHAIRMAN MALMUD: And, therefore, it was specific to the dosage.

MEMBER WEIL: Just to dosage.

CHAIRMAN MALMUD: The dose calibrator would not be intended to detect the wrong isotope, although it -

MEMBER WEIL: But it would.

CHAIRMAN MALMUD: - would by accident, yes. We discussed that, but we did ask for - do you want to broaden the request to incorrect pharmaceutical -

MEMBER WEIL: If that's feasible.

MR. EINBERG: It is feasible.

MS. HOLIDAY: Okay.

MR. EINBERG: We're already doing this preliminary -

CHAIRMAN MALMUD: Might as well.

MR. EINBERG: We're already looking at some preliminary numbers, but we don't have the capability in-house to do a detailed search. So, we're going to - but in the past 10 years there has been 650 human errors.

And so, from that we need to refine the dosage in isotopes.

MEMBER WEIL: Ten years?

MR. EINBERG: Ten years. And that's a preliminary number.

MS. COCKERHAM: Dr. Malmud?

CHAIRMAN MALMUD: Yes.

MS. COCKERHAM: Could I just ask Ms. Weil if their revision on the screen reflects what you - the clarification now?

MR. EINBERG: Can you read it for us?

MS. COCKERHAM: Sure. It says Dr. Malmud asked NRC staff to find data on events in which the radiopharmacy has dispensed the incorrect amounts of a radiopharmaceutical or the incorrect radiopharmaceutical.

CHAIRMAN MALMUD: Thank you.

MS. HOLIDAY: Okay. Moving on to Item 7, the ACMUI recommends licensing radium-223 dichloride under 10 CFR 35.300 and recommends, but does not recommend requiring direct measurement of activity before and after administration.

CHAIRMAN MALMUD: Correct.

MS. HOLIDAY: Okay. Moving on to Item 8, the ACMUI endorses the Committee report that was submitted on July 16th, 2012 with the following changes. We just wanted to make sure we captured this in open form directly what we wanted to change in the report.

Number 1 was recommend licensing of radium-223 dichloride under 10 CFR 300 and recommend, but not require, direct measurement of activity before and after administration.

Number 2, remove statement regarding applicability of report for all future alpha-emitting particles.

And Number 3, remove the statement regarding radium-223 dichloride significantly prolonging survival. The ACMUI will submit a report to the NRC staff with the aforementioned changes.

CHAIRMAN MALMUD: We all agree.

MS. HOLIDAY: Okay. Moving on to Item 9, the ACMUI requested that the reporting structure reviews

remain on an annual basis.

CHAIRMAN MALMUD: Correct.

MS. HOLIDAY: Okay. Moving on to Item 10, today Dr. Malmud created a subcommittee to review the refined abnormal occurrence criteria and provide recommendations to NRC staff.

The subcommittee members include Dr. Langhorst as the chair - oh, I'm sorry, that's supposed to be Ms. Bailey, Ms. Weil, Drs. Palestro, Dr. Welsh, Dr. Thomadsen and Mr. Mattmuller. The NRC staff resource person will be Ms. Angela McIntosh.

CHAIRMAN MALMUD: That is correct.

MS. HOLIDAY: Okay. And our last item is Dr. Langhorst asked NRC staff to provide direction as to whether or not the trigger criteria needs to be a part of the abnormal occurrence criteria, or if the trigger criteria could be used separately.

Did I capture that correctly?

CHAIRMAN MALMUD: That's correct.

MEMBER LANGHORST: Yes.

MS. HOLIDAY: Okay. And then of course the last item which has not been entered yet is that we have proposed that the spring 2013 meeting date will be April 15th and 16th, with a backup date of April 29th and 30th.

CHAIRMAN MALMUD: Correct.

MS. HOLIDAY: Okay. So, now I just want to touch upon the last bit of administrative items. For those of you who did not submit a financial disclosure form, I will send you the address via email.

At this time, could you remove your name tags? I will need those for the next meeting. And, also, could you write down your hours for the pay period so that I can submit that as well? And that concludes my presentation.

(Discussion off the record.)

CHAIRMAN MALMUD: If there are no other items for presentation, we will adjourn the meeting to meet again in April on the dates we have determined to be dates set, and the backup date as well. Thank you all. I thank you all for your participation and presentations. Thank you, and have a safe trip home. Look forward to seeing you at the next meeting.

(Whereupon, the above-entitled matter went off the record at 12:36 p.m.)