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UNITED STATES OF AMERICA

NUCLEAR REGULATORY COMMISSION

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ADVISORY COMMITTEE ON THE

MEDICAL USES OF ISOTOPES

(ACMUI)

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WEDNESDAY,

MAY 21, 2003

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ROCKVILLE, MARYLAND

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The Advisory Committee met at the Nuclear Regulatory Commission, Two White Flint North, Room T2B3, 11545 Rockville Pike, at 8:00 a.m., Dr. Manuel Cerqueira, Chairman, presiding.

COMMITTEE MEMBERS PRESENT:

MANUEL D. CERQUEIRA, M.D.	Chairman
JEFFREY A. BRINKER, M.D.	Member
DAVID A. DIAMOND, M.D.	Member
DOUGLAS F. EGGLI, M.D.	Member
NEKITA HOBSON	Member
RALPH P. LIETO	Member
LEON S. MALMUD, M.D.	Member
RUTH MCBURNEY	Member

COMMITTEE MEMBERS PRESENT: (CONT.)

SUBIR NAG, M.D.	Member
SALLY WAGNER SCHWARZ	Member
RICHARD J. VETTER, Ph.D.	Member
JEFFREY F. WILLIAMSON, Ph.D.	Member

ALSO PRESENT:

THOMAS ESSIG	Des. Fed. Off., NRC/NMSS
ROBERT L. AYRES, Ph.D.	NRC/NMSS
DONNA-BETH HOWE, Ph.D.	NRC/NMSS
MICHAEL T. MARKLEY	NRC/NMSS
CHARLES L. MILLER, Ph.D.	NRC/IMNS
ROBERT TORRES	NRC/NMSS
ANGELA WILLIAMSON	NRC/NMSS
RONALD ZELAC, Ph.D.	NRC/NMSS

AGENDA ITEM

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

8:08 a.m.

CHAIRMAN CERQUEIRA: Good morning. The first item on the agenda is review of "complicated" licensing issues since 10/24/02, and Dr. Donna-Beth Howe will be presenting.

DR. HOWE: Thank you.

MR. ESSIG: And while she is taking the podium, I just want to mention that because of condition orange, we now have escorting requirements for members of the public, so we'll have to probably, I noticed our audience today is a little bit smaller than yesterday, and it may be that some people are held down at the lobby, so we'll have staff go down and check periodically.

CHAIRMAN CERQUEIRA: The whole way coming up here, when you go by Bethesda Naval Hospital and the NIH, there's long lines of security checks to get in.

DR. HOWE: My topic today is basically a summary of some of the cases that we have handled here in headquarters that have come in from the regions, and most of them deal with the implementation of the new Part 35, and although I have one that is a carry over from the old 35. And what I'm going to be doing today is essentially just giving you a brief update on cases. I'll be talking

about the first four items.

The first one, strontium-90 eye applicator paces, intravascular brachytherapy physicist and then we have training and experience for board certified position, and he was board certified much greater than seven years prior and had not been in the field or on any license in about 26 years. And then the old case that we had was an exemption that we wrote to allow a licensee to give up to two rem for certain family members, for certain medical treatment. And the last group will be addressing issues of the physical presence of gamma knives and Bob Ayres will be handling those cases. So those are the ones I like the best.

Now, for the strontium eye applicators, when we revised Part 35, we did a number of things. One, we said that you have to have sources that are calibrated prior to -- they have to be calibrated in accordance with the new regulations before you can use them after October 24th. Most of our eye applicators are down in Puerto Rico, and we did a special stakeholder meeting in the end of September, and that's when some of our Puerto Rican physicians realized that they had sources that did not meet this criteria and needed to be calibrated.

So they did some fast scrambling to get their sources calibrated and they found out that there

was a waiting list. So they were doing everything they could to get them calibrated, but they had to wait for transport.

Yes, Jeff, you haven't let me get very far.

DR. WILLIAMSON: Well, yes, I was wondering if you could clarify what the detailed technical requirement for calibration is. This is a calibration by NIST?

DR. HOWE: The requirements are in 35.432, and that says that they're not -- I think they have to be essentially NIST-traceable, but it does not have to be done by NIST.

DR. WILLIAMSON: It could be done by ADCL then?

DR. HOWE: But for strontium eye applicators, I believe, there are only possibly two commercial facilities in the country that can do it, and then there is NIST, and so there's not a lot of options. And so the problem was that the physician wanted to continue treating patients while she was on the waiting list to get the transport package so she could send her source off for calibration, and we thought that was a reasonable request, and it was going to be a limited time, so we granted an exemption on her license for her to continue treatment for 90 days while she was waiting

to send the source off.

Now, it ends up if you had your source strontium-90 eye applicator calibrated, I believe, between 1990/1991 and 2002, the calibration procedures if you went to the right place, would have met the new Part 35. So not everybody had to get their sources calibrated, but most people did.

Our second case was a physicist that was a consultant to a number of licensees in Puerto Rico and the other thing we did for the strontium eye applicators is we had a tremendous number of misadministrations, and the misadministrations were based on improper calculation of decay, and so in the regulations we kept for the physicians the same as it had been before, but we require an authorized medical physicist to perform the decay calculations. And this particular consultant was a physicist. He was capable of making the decay corrections, but he did not meet the qualifications for an authorized medical physicist, so they sent in a request to have him listed as an authorized medical physicist with alternate training.

I brought this to the ACMUI. The ACMUI decided that yes, he was qualified to do the decay corrections, but no, he wasn't qualified to be an authorized medical physicist. So we granted an

exemption, and you'll see at the back of the slide, you'll actually see the wording of our exemption. And in this case, an exemption is always notwithstanding, and you state the regulation, and then you state what you are allowing them to do. And essentially, we allowed this individual to calculate the activity of the licensee strontium-90 sources, so they could be used to determine treatment ties for ophthalmic treatments.

Since we granted this exemption, the same individual has, with the same exemption, been listed on several more licenses in Puerto Rico, but we haven't had a request for anyone else to come under this. Okay.

Now, my second category intravascular brachytherapy. We had a request from our limited specific licensee to have an authorized medical physicist working as a consultant to them, but not at their location. Their authorized medical physicist moved eight to 10 hours away, and they believe that they really did not need him on site and they were using the Novoste unit, they considered it to be pretty much routine. You could follow charts that he provided, and therefore they wanted to use him as a consultant connected by telephone or email or fax.

And we looked at this and their license authorized them for intravascular brachytherapy, which

has a lot of different complicated issues associated with it. It does not restrict you to the simple labeling on the package insert, and we looked at the concept of consultant, and we decided that we considered the consultant to be someone that was actively involved, actively participating in treatment planning and subsequent treatment planning verification on each individual treatment plan.

And we believe for the wide variety of intravascular brachytherapy procedures that they were authorized to provide, that it was important to have the expertise for the authorized medical physicist there at the site, and this was not something that could be handled by telephone or email. So we would have denied the request, so this is the active participation, and this is the concept of the complex cases.

It ends up that they did get an authorized medical physicist that would be at their site, and so the question became moot. We did look to see if there were any cases in which we would have accepted an off site authorized medical physicist, and we decided that if they were limited to the package insert, which would have been the simpler procedures that were well-defined, did not require a lot of judgement from the medical physicists in trying to understand things, that that might be

acceptable. But we did not grant an exemption to this license.

Yes, Dr. Nag?

DR. NAG: On that circumstance, was that an authorized user? And if so, the physical presence part by the authorized user be that, because it's in the physical presence of the authorized user or medical physicist?

DR. HOWE: I think in this case, the authorized user was not going to be there all the time.

DR. NAG: Oh.

DR. HOWE: And they were just going to go with the cardiologist and use the authorized medical physicist as a remote location. Jeff?

DR. WILLIAMSON: Well, I thought the guidance was fairly clear that it was either the authorized user or authorized medical physicist that had to be physically present. And at least for this particular device, the Novoste device, I think it would be -- my view would be it would be extremely imprudent not to adhere to that requirement, even for simple cases. And one reason I would give you is this device has, I think, compared to other devices in radiation oncology, they're similar, extremely high failure rate.

DR. HOWE: We have over --

DR. WILLIAMSON: There's many, many medical events and misadministrations. I personally have been involved in some. The sources stick the fluid doesn't push them all the way. I think to comply with the -- to properly manage those incidents, I think really requires, I would say, certainly a physicist on site. You know, if for no other reason than to reconstruct the situation quickly and figure out what happened. And I certainly think that with just a cardiologist physically present, that's very bad safety practice for this particular device.

DR. HOWE: Okay. Right now, we're probably approaching 100 on medical events and device failures with the Novoste device.

DR. WILLIAMSON: I don't understand how you can, you know, accept not requiring one of those individuals to be there.

DR. HOWE: Okay.

DR. WILLIAMSON: And if the authorized users need to be there, I really question the wisdom of even in simple cases for the Novoste device letting the consulting physicist be eight or 10 hours away.

DR. HOWE: Okay, it's a good point.

CHAIRMAN CERQUEIRA: I think eight to 10 hours driving time, you know, it's fairly broad.

DR. BRINKER: I was going to ask pretty much the same question, because this is precedent- setting. On the other hand, of the 100 cases that you have reported, have any of them actually resulted in a dangerous over exposure to the patient?

DR. HOWE: In some cases, because the sources were lost, they were somewhere in the tube, and not identifiable, we've had significant exposures to other than the treatment site. In most cases, more recently with the smaller French units, there's kinking and the source doesn't get to where it is supposed to and if it is recognized fast enough or when the dummy goes out, then it ends up that the patient is on the table. They have to pull the whole device out and then they've had to go to alternative methods or alternative units.

CHAIRMAN CERQUEIRA: Yes, this topic is going to come up later today, but, Jeff, 10 hours away for a physicist, is that something that is supported?

DR. BRINKER: No, I think that the concept we sort of all agreed on that was appropriate was two of the three people that make up the team be there, and there be acknowledgement by the third person that that was okay, and that there would be the one interventional cardiologist and one radiation specialist be the authorized user of it.

CHAIRMAN CERQUEIRA: Medical physicist.

DR. BRINKER: On the other hand, and I don't know whether this pertained to this particular situation, the company has been very good at supplying their own personnel to assist in many of these cases. And they sort of suggest that that level of help, although they may not publish this, they suggest that that level of help is adequate with a trained team.

CHAIRMAN CERQUEIRA: Right. But is that trained person a medical physicist?

DR. BRINKER: No.

CHAIRMAN CERQUEIRA: I mean, so that -- okay.

DR. WILLIAMSON: It's not guaranteed by licensed condition.

DR. BRINKER: Yes, yes.

DR. WILLIAMSON: So their stock could go down next week and they might stop doing this.

DR. BRINKER: Yes.

DR. HOWE: And we also have medical events with their trained person right there.

DR. BRINKER: Well, there must be -- but I agree with the way things are now, and I don't think there is evidence to change that. But of the 100 events all of them, I presume, occurred with at least a medical

physicist and possibly a medical physicist and a radiation oncologist, so the presence of these people isn't going to preclude the event. It's just a safety factor for the appropriate handling of the event over and above.

DR. HOWE: And it makes it easier to go back and reconstruct what happened and determine what the doses were in the treatment sites, etcetera.

DR. WILLIAMSON: Right. I would think --

DR. HOWE: That's the major part. If you've got the person there and he is actively involved, he or she, then the ability to reconstruct is so much --

CHAIRMAN CERQUEIRA: Is so much better.

DR. HOWE: Right, better.

CHAIRMAN CERQUEIRA: And I think it's pretty uniform agreement.

DR. NAG: Yes, I think the major thing in that situation is that (A) they probably have to show us making sure that not lead to further exposure and danger in the lab. The other thing I wanted to ask this having the presence of two out of the three, if we extend it, then can we have the procedure go on with the radiation oncologist and the physicist being there, the radiation oncologist having seen quite a few of these cardiac caths being done with the gas on the floor without the

intervention of the cardiologist being there, and someone from the company could be there wishing oh, yes, you need to go a little further. Is that okay?

DR. BRINKER: Well, the reality is that if the catheter is placed already by an interventional cardiologist --

DR. NAG: No. The radiation oncology puts it in.

DR. BRINKER: Or radiation --

CHAIRMAN CERQUEIRA: Maybe we should table this discussion, because it's going to come up later on, and there will be enough discussion on it. But I think certainly the last item, you know, might consider with license authorization restricted to simple procedures, I think that's something that should come to this Committee for review before, you know, staff makes a decision, because there's been a lot of discussion and controversy. And I think certainly that's something that this Committee has a lot of interest in.

DR. HOWE: Okay.

CHAIRMAN CERQUEIRA: We'll come back to this. There will be plenty more discussion. But why don't we go on to the next step?

DR. WILLIAMSON: I just wanted to add procedural-wise.

CHAIRMAN CERQUEIRA: A quick comment. Okay.

DR. WILLIAMSON: I mean, I think, if there's a consensus we should affirm this policy. Maybe we should just have that on record, the authorized user or medical physicist.

CHAIRMAN CERQUEIRA: Well, that again, you know, we've gotten a lot of stuff. I think this will come up later on, and that might be the more appropriate place to discuss it.

DR. HOWE: Okay. Our next case was essentially a licensee came in and they were using the notification process, 35.14, which says that you can just notify the NRC within 30 days that you allow an authorized user, authorized medical physicist, authorized nuclear pharmacist work at your facility provided they meet certain criteria. And in this case, there are two important criteria. One is board certification, but the board certification authorization has an and, board certification and recentness of training.

The other alternative is if they are already listed on a license, and that's a present tense, so they must be listed on a license. Now, being listed on a license in NRC terms also includes being listed on a permit by a broad-scope licensee or being listed on a

permit by a master materials license or a permit by a master materials license broad-scope permit. So if you are recognized by either your broad-scope as being on a permit as an authorized user or by the regulatory agency, either Agreement State or NRC or the master materials license as being an authorized user, then you automatically can use this notification process.

In this particular case, the individual was not listed on a license. They had not practiced. They were board certified 26 years ago.

CHAIRMAN CERQUEIRA: Board certified in?

DR. HOWE: I don't have it here, but they want it to be 100 or 200 uses. The board certification was acceptable for 100 to 200 uses, but they were board certified in 1976.

DR. NAG: When was the last time they practice any of these procedures?

DR. HOWE: They were never listed on a license. They did not practice in nuclear medicine not to board certification.

CHAIRMAN CERQUEIRA: Did they provide any evidence of ongoing activity or CME?

DR. HOWE: No, no.

CHAIRMAN CERQUEIRA: Okay.

DR. HOWE: They move into more --

CHAIRMAN CERQUEIRA: So it seems pretty clear cut that this person does not qualify.

DR. HOWE: Right. And so the question was can you use 35.14, and the answer is no, you can't use 35.14. He is not listed on a license. He meets board certification, but doesn't meet the recentness of training and experience.

The next question is can the licensee make a determination of what is adequate alternative continuing training and experience or does the NRC? We went to the, I call them the Statements Consideration, but there's another term for them, it's in the beginning of the new Part 35, and that specifies that essentially the training and experience will be considered on a case-by-case, and we may bring it to the ACMUI as we deem necessary. That indicated to us that NRC is the one that makes the determination of whether it is adequate and not the licensee. So it's case-by-case.

And the next question is what do you use for criteria? And we thought about that and we said well, we really got pretty good criteria out there. Part 35 has just gone through a major rule-making. The medical community, the ACMUI, the staff has agreed that if you're coming the alternative route, there are certain items that you need to know about in radiation safety. And

they are listed for each type of authorized user, authorized medical physicist and authorized nuclear pharmacist.

So we're going to use those elements, not the hours, but the elements. And so what we would require would be that the licensee who wants this individual to be an authorized user, come back to us and give us evidence that this person is competent in those elements, and has continuing training and experience in those elements. So for this individual, we went back and said we also want to know -- radiation hasn't changed since '76. But the pharmaceuticals that are being used in nuclear medicine certainly have changed since '76. And so we asked that there be some evidence that they have current training in the new pharmaceuticals that have evolved since then. So that's the criteria we're using.

CHAIRMAN CERQUEIRA: Well, I'm not sure that this person would even meet most hospital, you know, privileging criterias to do the procedures. It would help in these situations to be a little bit more specific. I suspect this is probably a nuclear medicine physician or a radiologist.

DR. BRINKER: Probably a radiologist.

CHAIRMAN CERQUEIRA: Yes.

DR. HOWE: Yes, he was pushed to the front in one that would count, but he had spent most of his life in radiology and in ultrasound.

CHAIRMAN CERQUEIRA: You know, again, I think that the NRC's role is to look at the issues of competency in radiation safety and the basic principles of physics haven't changed that much, but somebody's knowledge base or awareness of things after 20-some years is deteriorated, and I, you know, am not sure I would spend more time on it. I think it is pretty clear cut that the Committee would support not granting. Now, quick comments.

DR. NAG: Yes, this person had 26 years, but I'm wondering is there anything, you know, that states when that person must have been board certified or anything like that?

DR. HOWE: No.

DR. NAG: Because I can foresee someone graduating, getting the boards, and maybe either going through some other kind of training for awhile or spending some time in research, and therefore did not apply for any license, and after five years you decide you apply for a license. How will we grant him that privilege?

DR. HOWE: The regulations in 35.59, I

believe you're familiar, say that your training and experience has to be obtained within the last seven years.

DR. NAG: Okay.

DR. HOWE: So if they went off for five years and came back, they would still be within that window.

DR. NAG: Okay.

CHAIRMAN CERQUEIRA: I think seven years or demonstrated CME or ongoing activity.

DR. HOWE: Right.

CHAIRMAN CERQUEIRA: Right.

DR. HOWE: But those seven years -- or demonstrate continuing --

CHAIRMAN CERQUEIRA: Medical education.

DR. HOWE: Yes. And a lot of times, just to make sure everybody doesn't get too excited about this, we consider if you're on a license and you're practicing, to be evidence of continuing, and so if you're on a license, then it's not seven years from when you got your board certification. It's from when the last time you were using licensed material.

CHAIRMAN CERQUEIRA: Right. Yes. Jeff?

DR. WILLIAMSON: Well, I guess I wanted to raise a general point about this recentness of training.

I think it's a difficult issue. Another issue I could imagine coming up is a radiation oncologist who is practicing in a facility say without cobalt-60 teletherapy for 15 years, and moves over to a licensee that has cobalt-60 teletherapy. And you know, I think that obviously they would fail this criteria, too, and I think it would be, you know, a serious mistake and injustice against that person's career to, say for example, insist that he or she repeat an entire residency.

DR. HOWE: No.

DR. WILLIAMSON: So I think it's important you have that.

DR. HOWE: No, we're not saying that you have to repeat a residency.

DR. WILLIAMSON: I understand. Let me finish.

DR. HOWE: Yes.

DR. WILLIAMSON: I think reasonable criteria how to catch-up training, I think, is important, but I'm not sure how this can be specified except on a case-by-case and discipline by discipline measure.

CHAIRMAN CERQUEIRA: And come back to this Committee, I think, is the reason.

DR. WILLIAMSON: And just the bottom line is

I think it would be prudent if you took advantage of the experience within this Committee to help you make these determinations and pulling it along.

CHAIRMAN CERQUEIRA: That's an excellent point. I think we'll approve of that.

DR. WILLIAMSON: This is really a --

CHAIRMAN CERQUEIRA: Why don't we go into the next case then?

DR. HOWE: Okay. My last case was we had a licensee that was treating children with, I think, it was MIBG and the licensee was to provide additional care for the child and to, they believed, give a better prognosis. They had the child interacting with the parents and they provided training to the parents. They provided pretty much the same instruction that you would provide to an occupational worker.

We had an inspection and realized that there were members of the general public that were exceeding the public dose limits for a patient that was hospitalized, and these children were hospitalized for their radiation treatment. So we had a violation and then the licensee came in and requested an exemption. About this time, we were working on the new 35 and the new 35 was going to take effect in about six months.

In the new 35 we had a provision that you

could receive up to 500 millirem with the authorized users okay in Part 20. So we felt that even though there was a violation of the regulations as they stood, when these doses were given, that we would use some discretionary action, and then the exemption request came in.

So all of the family members, at this point, had received under 500 millirem, so they would have been covered in the future with the new change to Part 20. But the licensee believed that they were having good results, and they wanted to up the amount of radioactivity they were giving to these children, and so they believed that they might be exceeding the 500 millirem level to the family members, so they came in and asked for an exemption up to two rem.

CHAIRMAN CERQUEIRA: Well, make them take the course.

DR. HOWE: Yes. Somehow you get into a drawing mode. I don't know how. The first point is it's not a generic case. This would be done on a case-by-case issue. We went to the Commission. The Commission was very clear. They want to be involved in these. So this is only for this particular license. If we get more requests similar to this, then we may have to consider rule-making, and then we certainly would be coming back

to the ACMUI. Yes?

DR. WILLIAMSON: I mean, this certainly seems like a reasonable request and it involves such a small number of people that it can be warranted. But when you say case-by-case, do you mean one patient case at a time or they would be allowed to do this perspectively for patients in similar position in their licensed practice?

DR. HOWE: No, they have an exemption that if they have the same kind of patient.

DR. WILLIAMSON: Yes.

DR. HOWE: Which are these young children receiving the same procedure and all of the family members receive the prescribed training and it is voluntary on the family members as to whether they provide the additional care and take the additional risk from the dose, then that's acceptable.

CHAIRMAN CERQUEIRA: Dr. Nag?

DR. NAG: Yes, I deal with this type of patient all the time. I do a lot of blood cell with children, so right before me, my suggestion would be that (A) with the right training to the family members and once they have the training, we, although legally they are members of the public, should use the same guidelines as for health care workers. Because (A) they are

providing care to that patient, their own child, the patient, so the limit should be the same as we would give to a health care worker.

DR. WILLIAMSON: Subir raises a really good point. These family members are effectively under the supervision of the radiation safety officer, now, they are badged and everything, so why is there even a need for --

DR. HOWE: But they're not --

DR. WILLIAMSON: -- an exemption?

DR. HOWE: -- employees of the licensee and couldn't be.

MR. MARKLEY: I worked on this exemption, so we ran into a problem with the lawyers. While the adult family members meet the definition of a radiation worker in the context of Part 19, they do not meet the criteria for an occupational worker in Part 20. It would require rule-making. So we ran into that hurdle with the lawyers. The licensee was not requesting a rule-making or generic thing, so we basically did the expedient thing. If we have additional case history, we did advise the Commission with a letter or a memorandum, rather, that if we have additional case history that we would -- that rule- making may be something we have to do down the road. But, at this point in time, we don't have that on

our plate.

DR. HOWE: And, Dr. Nag, if you're in an NRC state, then you can, on a case-by-case basis, allow visitors up to 500 millirem. But if you go beyond that, you're going to need --

DR. NAG: Well, we had --

CHAIRMAN CERQUEIRA: Dr. Eggli, you wanted to make a comment?

DR. EGGLI: Okay. I think it's important to understand how young these children are. The average neuroblastoma for which this child was treated is in the age of 2 to 4 years of age. And, in fact, not allowing the parents to provide care to that child would create a far greater public safety risk than any risk allowing the parent or care giver in the room could conceivably cause. So I think this is a very prudent and useful exemption.

DR. HOWE: And that was one of the primary supporting reasons that the exemption was granted.

MR. MARKLEY: That was fundamental to the licensee's argument and it was a strong basis for why we approved it, that the parents in this particular scenario are fundamental to the primary care of the child.

DR. NAG: Yes, I mean, I would like to go further, rather than having exempting like on a case- by-case basis. I would like to extend it to making those

that -- many people are not aware about that. So at that point, they may say oh, this is too young of a child, we cannot give this treatment to that patient. Whereas, if this becomes a part of the law that if a member of the general public is or has to take care of that child, then, you know, they can receive the radiation safety training and therefore then it would be same as an occupational worker. That would extend this treatment to a large number of people.

DR. HOWE: Well, I think that, at this particular point, we have difficulty with that, because the licensee that we granted the exemption to providing the treatment that they were providing before never exceeded 500 millirem, which is currently in Part 20.

DR. NAG: Yes, but that is only MIBG, and use low does-rate brachytherapy where the exposure would be, you know, more than .5 millirem. Many people are not giving those treatment at that interval low dose-rate brachytherapy at most hospital, but most doctors don't give it, because of all the regulation issues. They say oh, you know, we will be going way above the regulation. We won't even consider that. And I know many people, many children, are not getting the radiotherapy because of that. We got around that by doing HDR. Rather than using low dose-rate, we are now doing high dose-rate, so

we've gotten around that.

CHAIRMAN CERQUEIRA: This seems more like a practice of medicine type thing, you know. I'm just not sure what --

DR. NAG: But the regulation says --

CHAIRMAN CERQUEIRA: I'm not sure whether the rule-making per se would -- is there enough of a medical demand? How often do you get a request like this?

DR. NAG: No, but the thing is --

CHAIRMAN CERQUEIRA: Right. No.

DR. HOWE: Hold on a second.

CHAIRMAN CERQUEIRA: Right, right. No, I understand what you're saying that perhaps people who could get treatment are not getting it.

DR. NAG: I'm not considered.

CHAIRMAN CERQUEIRA: But I think the rule-making per se is not going to change the practice of medicine.

DR. NAG: But let one of the radiation oncologists --

DR. HOWE: I will point out that we --

DR. NAG: David, do you have any -- I know you probably don't treat children, but do you have any thoughts?

DR. DIAMOND: No, actually, I am a POG, Pediatric Oncology Group, investigator, but very, very rarely do we have a situation where we are considering using low dose-rate brachytherapy. Occasionally, we'll do HDR brachytherapy for soft-tissue sarcoma in a young teen or someone like that. So I have never had to face this issue. Particularly, now again, I am not exclusively a pediatric oncologist, so I can't give you a more thorough answer.

Certainly in the case the data presented, you know, this is a procedure that can't be done at more than two or three hospitals in the United States each year for neuroblastoma very selected patients. So I think the point that the Chairman raised is what is the demand? And I can't think it is more than just a handful of cases in the United States per year. And the question therefore is is this something that would best be served on a case-by-case exemption or is there a true need to go through an entire rules-making process? Perhaps just making those very few specialists, aware that may have a need for it, aware that this exemption exists, maybe that would satisfy things.

CHAIRMAN CERQUEIRA: I think that's probably would --

DR. HOWE: Yes.

CHAIRMAN CERQUEIRA: -- would be the best way to handle it.

DR. NAG: Yes, I think that would help, yes.

CHAIRMAN CERQUEIRA: Excellent? Next item?

DR. HOWE: That completes my talk.

CHAIRMAN CERQUEIRA: Okay. So we actually got done early. Boy, that's unusual, but I kind of -- you know, if we had agenda items and we have got outside people that are coming, I hate to jump ahead. I guess the next think is "Physical Presence Requirements During Stereotactic Radiosurgery Treatments," and we don't know who the interested parties are, do we?

DR. NAG: Yes. I mean, I know.

DR. HOWE: They're here.

CHAIRMAN CERQUEIRA: Are they here?

DR. NAG: Yes, they are here.

CHAIRMAN CERQUEIRA: Okay. So, Tom, should we go ahead?

MR. ESSIG: I think I saw enough yeses out in the audience, so that we could proceed.

CHAIRMAN CERQUEIRA: And Dr. Wilson and Tripuraneni would like to make statements, at some point, after the original, and the presentation, the soon to retire, Dr. Ayres.

DR. AYRES: Well, actually yesterday.

DR. NAG: Oh, okay.

DR. AYRES: Now, that the cat's out of the bag. All right. I also hope to finish far earlier.

CHAIRMAN CERQUEIRA: Microphone.

DR. AYRES: Oh, okay.

CHAIRMAN CERQUEIRA: Give him a level there, Mike.

DR. AYRES: I can sit down.

MR. ESSIG: Donna-Beth, did you walk off with the microphone?

DR. AYRES: I usually talk loud enough. I understand. Okay. Now, I'm wired. I am here to talk about the physical requirements, presence requirements for stereotactic radiosurgery. Oops. I'm just getting sorted out. The rule for establishing the physical presence requirements in the Part 35 is 35.615(f)(3). It's buried down into all of the various safety procedures associated with this modality, and the rule requires the physical presence throughout all patient treatments involving gamma stereotactic radiosurgery, why don't I just go to gamma knife, of both the authorized user and the authorized medical physicist.

Well, that is a rule requirement. Is there any way around that? We have gotten a couple of exemption requests, and that is why I'm talking about

this. We have received three sets of requests, one of which was approved and two requests that were denied, and I believe the actual technical assistance request, which is the headquarters response to these requests are a part of your package, and so all the details are there as, obviously, I'm just going to summarize.

How do we handle exemptions? Well, Part 35 also has a rule on granting exemptions, which states the Commission may, upon application of any interested person, grant exemptions from the regulations in Part 35. Donna-Beth's recent discussion of the two R limit is one classic case of that also, that it determines are, one, authorized by law and, two, will not endanger either life, property or the common defense and security, which is something that has gotten more attention lately and last, are otherwise in the public interest.

Well, how does the staff look at this when we receive an exemption request for a regulatory requirement, and that is in general for us to grant approval for such an exemption to the Part 35 requirements? The applicant must first, of course, provide an alternative or justification for the requested exemption from the specific rule requirements, and then when the staff reviews that, we must determine that there is an equivalent level of protection provided by the

proposed alternative, as provided in the rule.

In other words, the rule has gone through all of the process. The rule-making, as you're familiar with, has been through an extensive review process in establishing the appropriate level of protection, and so we treat the rule as providing that as it should be, providing the necessary level of protection. When we look at exemptions, do they do the equivalent? If it's yes, we'll grant the exemption. If it's no, we'll deny it.

So looking at some specific exemption requests, the first one, the alternative the licensee presented, they will meet the part of the rule requirement of having the physical presence of the authorized medical physicist. What they wanted to do as an alternative to the required presence of the authorized user was provide the presence, they would have both an authorized user and a neurosurgeon that in addition to being a neurosurgeon formally trained in the gamma knife procedures and radiation safety procedures present the treatment.

They would both be present at the initiation of the patient treatment and after that, the gamma knife trained neurosurgeon would fill the physical presence requirement for the continuing patient treatment. Now,

we deemed that we had the basis elements of the rule satisfied and that we had an appropriately trained physician and an appropriately trained authorized medical physicist present, and we granted this request for an exemption.

DR. NAG: Bob?

DR. AYRES: Yes?

DR. NAG: I have one question. Where would the authorized user be, in the building, but not physically placing --

DR. AYRES: They have got to be --

DR. NAG: -- or out of the building or out of the state?

DR. AYRES: They have got to be present right at the patient treatment site, generally the ~~council~~ consul.

DR. NAG: No, no, no, when you write the exemption, the day when they make that requirement.

DR. AYRES: We have no requirement.

DR. NAG: Oh, so they could be out of the building?

DR. AYRES: Well, it's not really. By the nature of their craft, it's highly unlikely, because they are going to be present at the initiation of the treatment.

DR. NAG: And be out of the building?

DR. AYRES: Well, certainly, they could be, yes.

DR. DIAMOND: Well, actually, Bob, that's not precise. I had a chance to discuss this with the individuals that wrote the exemption.

DR. AYRES: Yes.

DR. DIAMOND: I think some specifics would be very useful for this discussion. This is a very busy gamma knives center in Kansas City. They have a nice reputation, and basically what they told me over the telephone and what they wrote in their initial letter to NRC is they were describing a situation whereby once the treatment started, they wanted to be able to go and see patients either down the hall or down the corridor. I'm not exactly sure. So they did not go and specify being outside of the building, per se. I think, however, that we still need to come back and talk about this question in detail. But to answer your question, Subir, they were going to be in the building.

DR. AYRES: Yes, I'm pretty sure. I mean, I know you're correct. That was not something that we used as a check off. Our main consideration there was that we had appropriately trained physicians and medical physicists.

CHAIRMAN CERQUEIRA: But this level of supervision issue does come up, and it's usually related to billing issues, and it's usually broken down into, you know, sort of general, direct and personal supervision with personal requiring that somebody be physically present at the site.

DR. AYRES: Right.

CHAIRMAN CERQUEIRA: Direct meaning that they be in the building and, you know, general meaning that they sort of oversee everything.

DR. AYRES: Right.

CHAIRMAN CERQUEIRA: And don't have to be in the area.

DR. AYRES: And those --

CHAIRMAN CERQUEIRA: So this may be useful to keep in the discussion.

DR. AYRES: And those vary depending on the modality.

CHAIRMAN CERQUEIRA: Right.

DR. WILLIAMSON: And in this same request, didn't they also agree that the authorized users would be present at least 50 percent of the time? Wasn't that something they were offering or was that a different case?

DR. AYRES: Well, I believe you're correct.

CHAIRMAN CERQUEIRA: Yes, yes.

DR. AYRES: But I am not sure that that would have been a necessary condition for granting this exemption. I was trying to hit the key points and not that -- you all have a copy of the TAR response.

DR. WILLIAMSON: Well, actually, it's a useful piece of information for us to understand the internal dynamics of this practice.

DR. AYRES: Yes. What I want to do is say what were the key components in approving or rejecting an exemption.

CHAIRMAN CERQUEIRA: Yes, why don't you do that for us?

DR. AYRES: Yes. The first disapproved request, a licensee proposed that, as an alternative, that they have two individuals trained in gamma stereotactic radio emergency procedures that be physically present during treatment, either an authorized user, an authorized medical physicist or a physician working under the supervision of an authorized user. The second individual would be an unspecified gamma stereotactic radiosurgery staff member.

CHAIRMAN CERQUEIRA: So go back to the -- so the third person is? Can you go back one?

DR. AYRES: Yes, I think I got to go, yes.

It was unspecified, so it was assumed, the way the request was written, it would be another one of the list of three individuals, nothing saying it couldn't be two.

DR. NAG: Unspecified could be a nurse, could be a student, could be, you know, someone who is just --

DR. AYRES: Yes, you couldn't really tell, so it's just one of the problems that would arise.

CHAIRMAN CERQUEIRA: Okay. So I guess the Committee, how do people feel about having a physician under the supervision of an authorized user? I don't know exactly what that means.

DR. WILLIAMSON: So probably like a resident, a technologist?

DR. AYRES: Probably.

DR. WILLIAMSON: Is what the minimum would be in this request?

DR. AYRES: Well, they didn't commit and they didn't provide the level of detail to determine that.

DR. WILLIAMSON: Okay.

CHAIRMAN CERQUEIRA: Leon?

DR. MALMUD: If the second individual, the physician working under the supervision of an authorized user is a resident or a fellow that will then get the

provider into difficulty with Medicare, because Medicare pays for the resident, or a fellow under the technical component of the procedure, and will not pay again for the professional component.

So though it's not our problem as part of the NRC to be concerned about the reimbursement issue, our guidelines should, hopefully, be consistent with the reimbursement guidelines, so that we don't wind up being the excuse for an argument that the NRC said it's okay when, in fact, Medicare says it is not okay, it is fraud and abuse.

So I think we should be careful in stating that if there is another physician working under the supervision of an AU, that it would not be a house officer. It would have to be someone who has completed training. The house officer certainly could be there, but not in lieu of someone who has finished training.

DR. AYRES: But the key point on this request, they didn't specify who it was. We don't know the background, so that level of scrutiny was not necessary. It was just they didn't provide the appropriate individual.

CHAIRMAN CERQUEIRA: So if under this scenario, you could both have the authorized user and the authorized medical physicist not being present, but you

could have a physician who is a resident supervising the second individual who is an unspecified GSR staff member?

DR. AYRES: Probably not the case, but in later requests, that's a possibility, yes.

CHAIRMAN CERQUEIRA: But potentially it could be.

DR. AYRES: Yes.

CHAIRMAN CERQUEIRA: And I think it could be.

DR. DIAMOND: Yes, you could have a pediatric resident.

CHAIRMAN CERQUEIRA: Yes.

DR. DIAMOND: As your staff member.

DR. NAG: Most likely it will be a technician, technologist.

CHAIRMAN CERQUEIRA: Well, it's this physician working under the --

DR. NAG: It will be the second individual.

DR. AYRES: The second individual.

CHAIRMAN CERQUEIRA: The second individual.

DR. NAG: That's right.

DR. AYRES: Well, except the second individual, they changed the wording to staff member, which even broadens it further.

CHAIRMAN CERQUEIRA: Okay. I'm sorry, you

can go on to the next line then.

DR. AYRES: Okay. The problems we found with this, that only two of the individuals out of the proposed list of three meets the requirements for physical presence in the rule, are both an authorized user and a medical physicist. The second proposed individual may not meet either requirement or neither requirement. They just didn't provide the level of detail necessary to determine that.

The licensee's proposal does not ensure that the cumulative level of training and experience provided will be equivalent to that established by the rule. Oh, we denied that request.

CHAIRMAN CERQUEIRA: So, I think, everybody is pretty much in agreement that, as proposed, it's not appropriate, you know, that that third person on the authorized user list is not truly authorized. Okay. Good. Next?

DR. AYRES: The next request comes from a licensee that has two gamma stereotactic radiosurgery units, and in a conversation I had with them a couple of weeks ago, I understand it's going to become three. What they did is they built a central treatment planning room that sits between the two treatment units, and they are linked to each of the treatment unit control room via a

remote viewing system, a two-way audio communications system and an emergency alarm system.

What the licensee requested was an exemption to the physical presence requirements for four authorized personnel during simultaneous use of both gamma stereotactic radiosurgery units.

DR. NAG: And the two units are how many miles apart?

DR. AYRES: They didn't provide a facility diagram, but I would say 50 feet.

DR. NAG: Okay.

DR. AYRES: 50 feet, 150 feet.

DR. NAG: Okay.

DR. AYRES: But it's all in one joining facility kind of thing.

DR. NAG: Okay. That's really important. It may be small, but very important.

DR. BRINKER: Why was this disapproved? Is this --

DR. AYRES: I'm going there. What the licensee proposed as an alternative for this was that a gamma stereotactic neurosurgeon trained and knowledgeable in gamma stereotactic radiosurgery unit operations and emergency procedures be one of the individuals, and then to have present at each operating control area, which is

what the rule requires, either an authorized user, an authorized medical physicist or a neurosurgeon, and the other required individual, whichever one of those three that's not present at the console, would be in the central planning room and provide coverage for both gamma stereotactic radiosurgery units. So as you can see, we don't come up with the required two individuals at each unit that is established by the rule, it's not equivalent.

DR. NAG: But in this case, what a different scenario.

DR. AYRES: Yes.

DR. NAG: In this case, if the two units are basically adjacent to each other and, you know, it depends on how far your control panel is, you could consider that central planning unit to be the control panel, so it depends. That's why I'm asking --

DR. AYRES: It's not.

DR. NAG: -- how far apart are they?

DR. AYRES: It's not. The individual has got to divide his attention, the half individual I will call it, because he is covering two units, has to divide his attention between those, doesn't have constant presence or overseeing of the treatment, which is the intent of the rule. We have had cases.

CHAIRMAN CERQUEIRA: Yes, but what is the likely scenario that both patients in the room are going to be getting treatment at the same exact time?

DR. AYRES: Well, that's why they asked for this exemption, so this exemption only applies in that case.

DR. NAG: See, what happens here is that treatment can go on for quite a long time and, therefore, you know, you need a lot of time when you're about to start, but then once you start it, yes, you're doing it right, but if you're like adjacent to each other, you know, the level of supervision is slightly different, I mean, you know, with that.

CHAIRMAN CERQUEIRA: Jeff Brinker?

DR. BRINKER: The difference between this disapproved application and the first one is that in the first one, there would be a physicist available during the entire time with the neurosurgeon, but the authorized user would only be there at the very initiation.

DR. AYRES: Well, actually, it would be authorized user or neurosurgeon after the approval process, yes.

DR. BRINKER: Right. Well, okay, one of those.

DR. AYRES: Yes.

DR. BRINKER: So the rule, as I understand it, then requires three people, and if you had two units like this, you would actually need six people?

DR. AYRES: No, the rule requires two people, the authorized user and the authorized medical physicist.

DR. BRINKER: Okay.

DR. AYRES: But the licensees are bringing in as an alternative, as an appropriately trained on the unit neurosurgeon to substitute for the authorized user, yes.

CHAIRMAN CERQUEIRA: Jeff?

DR. WILLIAMSON: Well, yes, I guess on the face of it, you know, I think we have to have more technical detail. This does not seem an unreasonable request that, you know, it seems that, you know, we should really -- NRC should really have justification that there is clearly, you know, a threat or question concerning accuracy of treatment and the safety of the patients if this is, you know, substantially increasing their operating costs to do it this way, but that is just my first comment.

So I think then some of the details I would like to know about is whether, for example, the physicist covering both procedures from the central treatment

planning room has access to the control panel information needed to oversee the safety?

DR. AYRES: No apparent -- that is not, apparently, the case, but NRC clearly has the justification, a rule requirement for physical presence. The licensees either comply with it or provide a reasonable alternative that establishes the same level of safety. We don't think this does.

CHAIRMAN CERQUEIRA: But the physical presence, you have got two adjacent rooms, control area in the middle, and, again, I don't understand fully what's involved in these procedures.

DR. AYRES: It's not a controller. It's a treatment planning area, and they have enhanced it being an observation area.

CHAIRMAN CERQUEIRA: But physically --

DR. AYRES: They have no controls there.

DR. NAG: You know, but they are adjacent rooms, right?

CHAIRMAN CERQUEIRA: I mean --

DR. AYRES: They didn't provide a facility diagram, but they are in close proximity to each other. I don't know how many doors you have to go through.

DR. NAG: Yes.

DR. AYRES: We didn't get to that level of

detail.

CHAIRMAN CERQUEIRA: But, again, for the physicist and the radiation oncologist, I mean, what could possibly go wrong where having somebody 30 feet away, that you couldn't get that person to come in and deal with any emergencies? It wouldn't be necessary.

DR. AYRES: Well, I'll give you an example.

CHAIRMAN CERQUEIRA: Well, let me -- I mean, Dr. Nag or David?

DR. DIAMOND: Yes. I happen to perform a lot of gamma knives stereotactic procedures. I actually am less troubled. If I were in your position, I would have approved this request and not approved the first request.

DR. NAG: Right.

DR. DIAMOND: And the reason is, again, this is all speculation, but I would assume this is a busy university center, probably one of the top two or three centers in the country, which has this type of volume to acquire two gamma knives operated ones. They will probably be Pittsburgh or so forth, and they probably have a central control room that they use for treatment planning and then immediately adjacent to it have the two gamma knife units with the control panels right there.

DR. AYRES: Right. So it's not a control

room that we're talking about. It's a treatment planning room.

DR. DIAMOND: A treatment planning room, which has been modified, so they probably have cameras there, as well.

DR. AYRES: That's correct.

DR. DIAMOND: And then from that central treatment planning room, again, to extend my speculation, probably immediately adjacent to that are the two units with their attendant control panels. I would assume the way you describe it with the units being 50 feet apart, that it would take all of 15 seconds to stand up from the central treatment planning room and make it to the control panel, God forbid there should be a problem.

So to me, that is a reasonable request that does not have any real impediment to the patient or the public health. In contradistinction, the first one simply to me is an exemption that allows a physician to go and conduct other business out of earshot of an ongoing high dose-rate teletherapy, you know, treatment, and that to me is much, much more concerning.

DR. NAG: Yes.

DR. DIAMOND: So had I been in your position, I probably would have decided differently, but again, this is speculation, because I do not have the

exact specifications how you outlined them.

DR. AYRES: Yes, well, it really does the same thing.

CHAIRMAN CERQUEIRA: Ralph, did you have a comment?

MR. LIETO: I just wanted to be sure I understand here. Are you saying each gamma knife control area, is it one of those three, a user, medical physicist or the neurosurgeon, it's one of those three or two of those three?

DR. AYRES: One of those three is at the console.

MR. LIETO: So you could potentially, and if I understand this right, just have neurosurgeons there?

DR. AYRES: Well, if we had pursued this and it looked reasonable enough, the two-person rule, we probably could have sorted this out. Their request wasn't clear on which individual would be where, and that we wouldn't get an overlap of, like you said, of two neurosurgeons or two medical physicists, but I think that was a minor issue and it could have been sorted out. What we didn't come up with is the equivalent of the two required individuals being present.

CHAIRMAN CERQUEIRA: But the two requiring -- and, again, the way this is described in terms of the

physical layout, I personally don't see a problem in the sense that I, you know, again, not doing these, I don't fully understand the potential emergency. But if you have got somebody that is 15 seconds away from the ability to intervene, that seems reasonable to me.

Jeff, what do you say?

DR. WILLIAMSON: Yes. I think that your approach is too rigid and takes the letter of the regulation too literally, and I think you should think about the details of the safety requirement that if there is an emergency, can the person in the control room detect it quickly and respond before a significant excess dose is given to any sites?

You know, I would have inquired about the details of exactly what information from the control panel do they need. Is it available in the treatment planning room? And I just think, in general, you have handled this in an unreasonable way, and this is exactly the kind of thing that NRC should avoid, and you should try to be a little more flexible when someone proposes an alternate that provides the level of safety needed.

CHAIRMAN CERQUEIRA: All right. So our two radiation oncologists, our medical physicists, seemed to feel that, you know, again, not knowing fully all the details, but certainly the way this particular unit was

laid out with two rooms with a central control area, with, you know, an appropriate person 15 seconds away from either room, that that would not, you know, endanger the staff, the patient or the public, then this would be acceptable.

Dr. Leon and then Jeffrey Brinker.

DR. MALMUD: I respectfully don't agree with Dr. Williamson, because you did pick up something that was important, and that is the way that that slide is presented, there may be no physicist present among the three people between the two rooms. Do you approve of having no physicist present for a gamma stereotactic radiosurgery?

DR. WILLIAMSON: No, I would not approve that aspect of it. I think I am addressing the generic issue of NRC forcing a busy center like this that has tried to design, I think, a multiple unit treatment facility to have two or three separate teams, I think, is an unrealistic demand. But I do think that if they had two units running, one of the people should be an authorized user and the other person should be an authorized medical physicist, especially in this setting.

DR. MALMUD: Well, then we agree, but the way it was presented, there could have been -- there would be no physicist theoretically present, and that is

how that is presented.

DR. WILLIAMSON: Yes.

DR. MALMUD: The first is a neurosurgeon, the second may be an AU, AMP or a neurosurgeon.

DR. WILLIAMSON: Yes.

DR. MALMUD: And the third, again, may be.

DR. WILLIAMSON: Well --

DR. MALMUD: I would be concerned. I have no problem in recommending that two rooms could be managed by three people, but then we would have to be rather a bit more specific about what constitutes those three people. Otherwise, the neurosurgeons, three of them can be there and there may be no one who has the physical background.

DR. WILLIAMSON: Your point is very well taken, and I would agree completely. I am, you know, basically criticizing the logic underlying this decision. I am very concerned about it.

CHAIRMAN CERQUEIRA: Well, Jeff, Dr. Brinker?

DR. BRINKER: I just think the issue of flexibility may be key here not only from the NRC's point of view, but from the licensee's point of view whether they would agree, for instance, to have the required radiation specialist in a reasonable number, but the

logic of approving the first one and not this one falls on their inflexibility to do that.

So the question I have for you is when you discuss something like this, you get a proposal like this, and you see it worded like this, do you say no, I can't do it or do you say well, how about we have already approved something where two people, one radiation specialist and a qualified neurosurgeon could work a room? What if we had something where, you know, a total of three radiation specialists and not four would be required? Do you offer compromise situations?

DR. AYRES: When you have explicit rule language, the rule language is either met or not met. Then we have an exemption and we compare it, does it rise to the equivalent level of protection or does it not?

CHAIRMAN CERQUEIRA: But I think we write some of the rules and we know that it can be subject to interpretation, and I think the bottom line is, you know, the safety issue, and I think, you know, again, people have bought into the concept that the way this particular unit was set up could run. There are issues about who you need there, but, Jeff, if something goes wrong and you need to do something, I mean, does the physicist need to come in and physically do something? Can the radiation oncologist do it?

DR. WILLIAMSON: Well, I think either the physicist or radiation oncologist or even a properly trained neurosurgeon could probably do the thing, which is, you know, stop the treatment and manually extract the patient from the machine.

CHAIRMAN CERQUEIRA: Pull him out.

DR. WILLIAMSON: But, you know, the requirement to have two sets of eyes is not an unreasonable one, so I think, you know --

CHAIRMAN CERQUEIRA: But four in this situation may be a little bit --

DR. WILLIAMSON: Well, for each treatment, you know.

CHAIRMAN CERQUEIRA: Right.

DR. WILLIAMSON: So I think, you know, many details, I think, would have to be explored in this, including how they make the required information regarding the progress of the treatment available in the treatment planning room.

CHAIRMAN CERQUEIRA: Right. Ruth?

MS. MCBURNEY: Just coming from a regulatory perspective, probably if we had been asked to do the same thing, we would have gone back to them and asked for more explicit information on who those people were that were going to be present where, and tie that down in the

license condition if we granted that exemption.

DR. AYRES: It's not on here and it's an important point.

MS. MCBURNEY: Right.

DR. AYRES: Since the technical assistance request reply was done, the licensee subsequently called me and we worked out what would work and they were quite happy with it.

DR. WILLIAMSON: And what was that?

DR. NAG: I think this is --

DR. AYRES: They didn't realize that they could substitute and appropriately train neurosurgeons as we approved in the first technical assistance request for an authorized user, so they were quite satisfied to be able to use a medical physicist and an authorized user and/or a trained neurosurgeon at each set of consoles, which may grow to three, at some point, so that would be six individuals.

DR. NAG: I think this may be rather good. I think, Dr. Tripuraneni, you may have some insight. We might have a decent oncology.

CHAIRMAN CERQUEIRA: Is this an appropriate time for you to come forward? Great. Well, why don't you -- do you want to take a seat up here, front and center? So you're going to make a statement related to

this?

DR. NAG: I think some comment related to the discussion we were having.

DR. TRIPURANENI: I think I'll come to that. Good morning. Thank you, Mr. Chairman and council members for giving me the opportunity to present this. My name is Prabhakar Tripuraneni. I am a radiation oncologist and head of radiation oncology at Scripps Clinic in La Jolla. I do about 50 gamma knife cases a year for the past five or six years, so I do have quite a bit of experience in the gamma knife, and I am actually representing ASTRO.

DR. AYRES: Can I interrupt?

DR. TRIPURANENI: Which is the professional organization of radiation oncologists, American Society of Therapeutic Radiology and Oncology. And, actually, we do have a written comment that actually has been provided to the ACMUI and, actually, available for, I guess, a few more copies in the back row.

We strongly agree with NRC position that both authorized user and authorized medical physicist be physically present during the delivery of the gamma knife. And gamma knife, as you know, uses almost 200 cobalt sources, and it actually delivers very high doses, single-dose radiation therapy to the brain.

Looking at some of the practicalities hearing the discussion right here, I think one of the concerns is that by not having both trained people, that is the authorized user, authorized medical physicist, if there is a problem that actually happens, how to prevent that.

In relation to that, having done many gamma knives, close to probably 300 plus there, the other important thing that actually happens is during the delivery of gamma knife, which typically takes anywhere between 30 to 90 minutes, I think Dr. Diamond can corroborate with that, that both typically the authorized user, authorized medical physicist and sometimes neurosurgeon actually checks all the parameters, the X-Y-Z quad, and it's actually what you are going to do for each shot.

And after doing about something like about three or four shots, it actually gets to be very mind numbing to looking at all these numbers, and I think it's a very critical part in actually setting those shots and often, if a mistake is made, it is usually not realized, because there is no computerized backup system set, at least for most of the gamma knives that are available, at this point, in the country.

So I think it's critically important that

the people that are trained, first the authorized user and the medical physicist and possibly sometimes the neurosurgeon, actually be there and actually check all these parameters actually during the treatment, and obviously be physically present to take care of any problems that might potentially happen right there. As Dr. Hendee said yesterday that the American Board of Radiology grants that license for the radiation oncologists and the medical physicist that actually go through the extensive training and the background.

At this point, I think the society's position is that, I think, we do strongly agree with the NRC position that both AU and AMP be present at the time of the treatment right there. And also, we commend them, especially the second request that actually has been declined.

The first request that actually was granted, the exemption, we do not think it's fair, because as it is written here, it says that the radiation oncologist or the authorized user be present for an average of about 50 percent of the time during the delivery of the treatment.

As I said, the typical treatment times are usually no more than 30 to 90 minutes average patient. Of the past 300 I have done, I would say it's probably in the 40 to 45 minute range, right in there. So we are

talking about giving an exemption of about 20 or 25 minutes for the convenience of the radiation oncologist that can go and do something else, and I think for a single high dose-rate, external beam radiation therapy, especially being delivered to the brain, for the safety of the patient, and we think actually that both of them should be there, AU and an AMP. Of course, there could be some extenuating circumstances where exemptions could be granted on a case-by-case basis. At this point, we are not willing to comment.

CHAIRMAN CERQUEIRA: Excellent. Thank you.

DR. NAG: No. Mr. Tripuraneni, that third case where you are having two adjacent rooms, you know, a radiation oncologist can go back and forth and still is seeing each shot being, you know, check on each shot.

DR. TRIPURANENI: I personally think that actually there should be a dedicated authorized medical physicist or an authorized user be present, dedicated for each patient in both rooms, and then I think that there should be a second person, likely to be the second authorized user or a neurosurgeon, should be there and I think you could have perhaps -- let's take an example.

I think you have two patients going on in two rooms simultaneously. I personally do not have any problem if there is an authorized medical physicist and

a trained neurosurgeon taking care of each patient in both rooms, and then an authorized user kind of covering both rooms. I personally would not have any problem doing that.

The typical gamma knife is laid out that the treatment planning system is in a different room, and right next to the gamma knife itself there is a small console area where you actually punch in all the numbers and check all the numbers right there. I think if there is one AU supervising both rooms, as long as there are two dedicated in doing this, AMP and a neurosurgeon, I personally would not have any problem and I would support that position.

CHAIRMAN CERQUEIRA: I guess I would come back to the issue, which is going to certainly come up with the cardiologist, you know, in terms of the treatment. You know, when you have got a patient were you, basically, have got a neurosurgeon present who is monitoring a patient and you have got issues of radiation safety, if you have got an authorized medical physicist, what does the radiation oncologist add to that particular situation in terms of, you know, overall clinical safety or radiation safety?

DR. TRIPURANENI: We understand. I think this question has come up many times. Once again, as Dr.

Hendee has suggested, I think the radiation oncologist, the authorized user has the training and the background to actually deal with the broad range of radiation safety issues. I do see your question that there is --

CHAIRMAN CERQUEIRA: Right. But most of those are sort of an acute management issue related to safety, and if you have an appropriately trained individual, and I guess both you and the NRC have said that an appropriately trained neurosurgeon appropriately, you know, in the aspects of the risks and how to avoid those risks in combination with the medical physicist, can appropriately monitor the situation. So do you disagree with that?

DR. TRIPURANENI: I disagree that treatments cannot be delivered by AMP and appropriately trained neurosurgeon only.

CHAIRMAN CERQUEIRA: For what reason is that?

DR. TRIPURANENI: Once again, I think radiation oncologist, the authorized user, who actually is prescribing the dose of radiation therapy, have looked at the plans and actually trained in the management of the patient.

CHAIRMAN CERQUEIRA: But the prescription, isn't that probably made by the physicist?

DR. TRIPURANENI: Absolutely not, Mr. Chairman.

DR. AYRES: No, probably by the radiation oncologist.

DR. TRIPURANENI: Radiation oncologist is the one who is actually looking at the patient. Let's say if you go to a gamma knife procedure, the neurosurgeon comes in and puts on the helmet, basically, the frame. Then typically, the patient gets either CT or MRI, and then the radiation oncologist and neurosurgeon often work together to draw the target volumes. Typically, three of them, both neurosurgeon, radiation oncologist and the medical physicist actually work together to come up with a plan.

Radiation oncologist actually prescribes the dose, at that point in time, not only the dose that you are going to deliver in the range of anywhere between 15 to 23 or 26 grade, it's a very small volume that could range anywhere from a fraction of a cubic centimeter or all the way to 20 to 30 cubic centimeters. And once that plan is approved by the radiation oncologist, obviously typically in consultation with the neurosurgeon, then you actually deliver the treatment.

It's a single high dose radiation therapy to the brain. In the beginning of gamma knife radiosurgery

back in 1970s, there have been many patients that actually developed a brain necrosis, because adequate care was not provided, especially we did not know this, but those programs and all those things --

CHAIRMAN CERQUEIRA: But the technique has evolved, I guess, to some extent. But, Jeff, you wanted to make a comment, eagerly raising your hand?

DR. WILLIAMSON: Yes, I have a couple questions, you know, and they concern two issues, so I think maybe the two issues regarding emergency response and, you know, accuracy of treatment involve the issue of setting and verifying the stereotactic frame coordinates.

Now, my understanding is is that stereotactic frames are a common practice tool in neurosurgery, and so your claim must reduce to the fact that only the radiation oncologist has the training to verify these coordinates and not the neurosurgeon, that a neurosurgeon who has had specific gamma knife training is not as competent as the radiation oncologist or cannot provide the level of accuracy and oversight to verify those coordinates.

So, is that correct, you're making that claim?

DR. TRIPURANENI: I don't think I quite said that, and I think the neurosurgeons are quite competent

in actually using the stereotactic framework, because they use that program. However, what is unique to gamma knife radiosurgery is that you do need to check those shots and check those X-Y-Z coordinates.

Typically, in neurosurgery, there are no circumstances, to my knowledge, that a neurosurgeon would have to check the X-Y-Z coordinates at 10 or 15 different times in a matter of 30 or 45 minutes, and I think that's fair. For this single high dose radiation therapy to the brain, I think you need to be as clear as possible, so that you are actually setting up these coordinates adequately, so you are giving the appropriate treatment.

CHAIRMAN CERQUEIRA: So what's involved in setting those coordinates? I mean, you know, what sort of knowledge base do you need or what?

DR. TRIPURANENI: It's the responsibility, and once again --

CHAIRMAN CERQUEIRA: Well, no, no. Well, responsibility, you know, what sort of knowledge do you need to set those coordinates? Why couldn't the neurosurgeon do that?

DR. TRIPURANENI: Oh, neurosurgeons do. Typically, what we'll do is when you are working with three sets of numbers, once again, you are looking at typically, let us say, 79.3 millimeters for the X

coordinates and 81.4 for the Y coordinate and 103.6, wherever, for the Z coordinate, and typically the practice in our gamma knife center is that typically all three of us are present even though we do acknowledge you don't need all three of them.

CHAIRMAN CERQUEIRA: But what is the technical radiation knowledge that you need to set those coordinates? Ralph?

MR. LIETO: You know, I would like to maybe give an analogy. I think that it's the body of knowledge that you're bringing and your understanding of the instrumentation and the equipment that goes on. I mean, you know, in nuclear medicine, I mean, you know, if you want to give an iodine therapy in a capsule form, you don't need a lot of technical knowledge to do that. Okay.

CHAIRMAN CERQUEIRA: Right.

MR. LIETO: You can get, you know, some student nurse to do that. But, I think, what you want --

CHAIRMAN CERQUEIRA: Leon?

MR. LIETO: Well, I mean, in terms of giving capsules. Well, I'm glad it kind of upset him, I mean, because I think that's sort of the analogy I wanted to make is that you want the people that can respond and are

knowledgeable about the modality, and you definitely need that type of person present.

DR. WILLIAMSON: Physically present to deliver an iodine capsule? I don't think that's covered in the regulations.

MR. LIETO: No, I was talking about the gamma knife.

DR. WILLIAMSON: You know, clearly, you need the expertise to give a prescription.

MR. LIETO: Actually, if there was an issue and the patients have questions and so forth, it shouldn't be a technologist or a physicist answering, you know, clinical questions for a patient. It should be your authorized user.

DR. WILLIAMSON: But that's not --

MR. LIETO: Well, they should be present and, you know, and available. Okay. But, I mean, in terms of trying to make an analogy about who is administering, I think it's a valid analogy.

DR. TRIPURANENI: I check the X-Y-Z coordinates. The other thing that I always do is I usually do a common sense checklist. Sometimes, the numbers could be very surprising. Sometimes, you treat this patient and still point out the front patient, and you could be off to the left side of the brain. You are

also centered on the right side of the brain.

CHAIRMAN CERQUEIRA: Right. But see, those are technical things that don't necessarily relate to radiation knowledge or awareness, yes. David?

DR. DIAMOND: I think we are getting off a little bit onto a tangent as to what training is necessary on checking stereotactic frame coordinates. Although, the point of independent quality assurance checks is extremely key, and that's obviously fundamental to any quality management program. I think the real issue, when I think about these issues, is that these patients are getting whopping doses of radiotherapy at extremely high dose-rates, and the underlying principle just from a simple perspective to my thinking is that these are my patients.

I have the ultimate responsibility to make sure this radiotherapy is delivered safely, and you better darn well believe that I am going to be there like a hawk the whole time and not divulge or divest that responsibility to anybody else. So that is how I approach this, and that is the fundamental thing. We're trying to make sure these patients are safe and we can go and kill a person very, very quickly.

We can train a lot of different individuals in actually how to go and remove a patient rapidly from

a unit. We can train a lot of individuals how to go and check frames and make sure that the treatment planning system is calibrated correctly, but in the final analysis, whether it be just from an ethical standpoint or from a point of law, I am responsible and there is no way on earth that I am not going to be there every second of this treatment, and that's an issue.

CHAIRMAN CERQUEIRA: So what is a neurosurgeon there doing all this time?

DR. DIAMOND: Well, quite obviously, we do it perhaps differently. We will have the neurosurgeon place the head frame, typically, very early in the morning, 6:00 a.m.

CHAIRMAN CERQUEIRA: So this is not a surgical procedure? You basically have this external cap?

DR. DIAMOND: It's a very minor surgical procedure. You know, sometimes I will help put the frame on.

CHAIRMAN CERQUEIRA: So brain surgery is minor surgical?

DR. DIAMOND: So it won't go too deep when I put it through the skull.

CHAIRMAN CERQUEIRA: Okay.

DR. DIAMOND: And let's say it's a patient

who has a very straightforward --

CHAIRMAN CERQUEIRA: Is the patient under general anesthesia?

DR. DIAMOND: No, no, no, we just do local.

CHAIRMAN CERQUEIRA: Awake, conscious patient?

DR. DIAMOND: For an example, for a trigeminal neuralgia patient, which generally involves a single shot, once we have together planned the treatment, checked the coordinates, initiated treatment, that neurosurgeon has no statutory requirement to be there, we'll let the patient go. I will remove the head frame. I would not ever think about leaving the room.

Now, in many cases, we do this very complex skull-based acoustic neuromas or arterial venous malformations that do involve 15 or 20 shots, so practically that neurosurgeon can't go off and do other business, but many times when we do do single shots or a renal cell carcinoma, solitary metastasis or a trigeminal neuralgia, which is a single four millimeter polymer shot, the neurosurgeon will go. There is no statutory requirement nor is there any real need for that patient, you know, provided the patient is stable.

CHAIRMAN CERQUEIRA: Good. That's --

DR. WILLIAMSON: But there are other

scenarios. At Washington University, I know the neurosurgeon is very involved with the radiation oncologist and physicist in doing the treatment planning.

DR. DIAMOND: Right. I was very careful to say that we are all intimately involved when doing planning.

DR. WILLIAMSON: So there are situations where, I think, you know, the knowledge base, at least in this narrow segment of activities on the neurosurgeon's part, you know, can be quite adequate, I think.

DR. DIAMOND: I missed something.

DR. WILLIAMSON: You know, my impression is, you know, at least in that one situation, the neurosurgeon has a very good understanding of the dynamics of the device and the coordinates and, you know, the details of how to read the treatment plan coordinates and confirm, you know, the machine settings, at least in that case.

DR. DIAMOND: Oh, I think all the neurosurgeons we work with have a good understanding of that, as well.

DR. WILLIAMSON: Well, it is one of their bread-and-butter instruments.

DR. DIAMOND: Sure.

CHAIRMAN CERQUEIRA: So they understand the

instrumentation and what needs to be done and the radiation things then? All right. Well, maybe we should bring Bob back up and, you know, we can let you sit at the table. Is that okay?

DR. MALMUD: I have a quick question I wanted to ask.

CHAIRMAN CERQUEIRA: Sure. Please. I have to let Michael, also.

DR. MALMUD: In the course of your comments, did I understand you to say that in the example that was cited before, the two rooms side by side with a central control or observation area, that you would recommend that five people be present, two in each room and one floating back and forth? Did I understand you correctly?

DR. TRIPURANENI: That's correct.

DR. MALMUD: Thank you. I think it was five, not three.

DR. TRIPURANENI: That's correct.

CHAIRMAN CERQUEIRA: Well, an authorized user, radiation oncologist floating back and forth between the two.

DR. TRIPURANENI: That was the specific example. I agree.

CHAIRMAN CERQUEIRA: Okay.

DR. AYRES: Well, I ended up with just the

last slide to go, which summarizes these things. The rule requirement is, as you mentioned, sometimes rules are subject to interpretation. The particular requirement for physical presence is not. I mean, that is a good example of being very clear, and it simply requires that the authorized user and the authorized medical physicist both be physically present throughout the treatment, and it's justified on the basis of the inherent risk of these procedures as Dr. Tripuraneni just talked about to some length, these are probably the most risky, and also Dr. Diamond, radiation therapy procedures there are if it goes wrong. It's a great procedure when it doesn't.

And they need to be available to respond in an emergency, and this could be a malfunction of some sort of just an actual medical emergency, and to ensure that the correct dose is delivered to the patient, and we have had several examples where either the authorized user or the neurosurgeon, we don't regulate the neurosurgeon, I think all three present is great and a preferred way, and that's the way I would like it if I was a patient, but where both have participated or the individual that was present participated in treatment planning knew what should have been happening and caught a misadministration, generally a wrong treatment site

because of reversed image, a wrong treatment plan was loaded.

You know, that don't look right. The numbers are right. The frame settings are right according to the treatment plan, but it's the wrong treatment plan. The physician's knowledge caught the ear before substantial damage was done. They bring a lot to the table. They need to be there.

DR. WILLIAMSON: Well, in none of the applications or at least in this case, certainly the authorized user is present or could be present at the initiation of treatment and, you know, I don't think anybody is arguing that the radiation oncologist should not be the authorized user and in charge and responsible for the treatment.

DR. AYRES: Well, in one of the examples I quoted, there would have been several shots delivered before this don't look right come up and it saves four or five more. It was a complex tumor treatment, and it was on the wrong side of the hemisphere of the brain.

But if we got in a mobile facility situation with shared control, that's a ripe opportunity for any individual or the public to petition for rule-making perhaps, but the rule as it exists right now is quite clear, two individuals the way we treat it, and the

exemption space is if the licensee wishes an exemption from the absolute rigid requirements of an authorized user and authorized medical physicist, they can come in with a proposal and we examine it on a basis of does it give the equivalent level of protection as the rule requires? And the three cases I presented illustrated in those specific cases how we did that. I was hoping to finish early. It wasn't quite as early as I thought.

CHAIRMAN CERQUEIRA: Well, yes, you did. Any further questions for Bob? Tom?

MR. ESSIG: If I'm permitted, I just wanted to ask a clarifying question, Bob. On that first disapproved request where we talked about the second individual, an unspecified GSR staff member, did we attempt to obtain from the licensee any more specificity? Is that the way the licensee wanted it? They didn't want to specify who that individual would be?

DR. AYRES: Well, we don't normally go back to the licensee. We'll deny it and then they can come back on the basis of the denial and try to reapply addressing those issues, but it's not common practice in NRC space that headquarter staff talk to the licensees. We get the request, assuming all the background work has been done by the region, and we're responding on these, not to the licensee, we're responding to the region.

MR. ESSIG: I just thought that should be provided.

DR. AYRES: I know you knew it, and I figured that's what you were looking for.

CHAIRMAN CERQUEIRA: Jeff, do you have a comment?

DR. WILLIAMSON: Yes, I have a question about this whole process. I mean, I think I would encourage NRC globally, the regions, the headquarters and so on to try and be a little more customer friendly in terms of negotiating with the licensee, somebody to try to help them solve the problem. Secondly, you know, I think these requests should have more specific technical information, and I think they should address the specific risks and safety issues more and, you know, I think this sort of whole presentation, from my point of view, has been too legalistic and attorney like and not focused enough really on the clinical and safety risks to the patient or there hasn't been, you know, discussions of the specific issues and the scenarios, time-motion studies and so on, how to respond to emergency situations when unusual staffing arrangements like this are contemplated.

DR. AYRES: And as Tom addressed, like I said, the regions communicate with the licensees

generally and we communicate through regions, and I mentioned we resolved the issue of the shared mobile facility by myself speaking to the licensee. How that happened is he called me on an issue of appearing here and presenting a position, and once we had the discussion, he decided that he didn't need to do that anymore.

CHAIRMAN CERQUEIRA: Now, Bob, at what point do you actually, you know, approach a committee member about some of these issues? I mean, you know, we have got two radiation oncologists. We have got several medical physicists.

DR. AYRES: If the rule is clear, why?

CHAIRMAN CERQUEIRA: Because the rule is subject to interpretation.

DR. AYRES: No, it isn't, not this one. I challenge you to interpret it.

DR. WILLIAMSON: Well, actually, Bob, the issue is that granting exemptions from your clear rules, so come on.

DR. AYRES: Well, does it provide an equivalent level of safety?

DR. NAG: But that's when you're acting like a policeman, rather than as a human being.

DR. AYRES: After hearing you it's no.

COURT REPORTER: I can't hear.

CHAIRMAN CERQUEIRA: Yes. All right. One person at a time. So, Jeff, you had a comment?

DR. BRINKER: Well, just a question; do you publish cases in which you either approve or disapprove exemptions?

DR. AYRES: No, the technical assistance requests are not public documents. We provided them to committee here on these three cases since we were talking about them.

DR. BRINKER: So that someone who thinks that they might qualify for an exemption has no ability to search out whether other people have gotten an exemption for a similar situation.

DR. AYRES: That's correct.

MR. LIETO: These don't go into -- excuse me, these don't go into ADAMS?

DR. AYRES: Not in the publicly available ADAMS, that's correct.

CHAIRMAN CERQUEIRA: All right, Niki?

MS. HOBSON: Well, I guess I'm stunned and appalled that the welfare of the patient really doesn't -- I mean, giving the patient the kind of care that's going to help cure the cancer seems to be way down on your priority list. Following the rules is more

important and I think that's kind of the wrong approach. Caring for the patient should be the top priority and if you can't accommodate giving good care to the patient with the rules then there's just something wrong with this system and the approach.

DR. AYRES: And I think we did just that by providing appropriate protection for the patient. And as Dr. Diamond says, he would always be present and I think that's our minimum expectation, that we always have an appropriately qualified physician present for these treatments. I went through the entire rulemaking process, is a rule, what we think is the right level.

CHAIRMAN CERQUEIRA: David?

DR. DIAMOND: Bob, I would like to add that speaking for myself and perhaps other members of the committee, we would welcome any input. We would welcome any input when you're trying to go and weigh in on these exemption requests as they come through. For example, I only found out about the Midwest Gamma Knife Center exemption request in a very serendipitous way. It would have been very helpful to me to have known about this and been able to give feedback. It would also have been very helpful in the two cases that you actually disapproved to provide feedback.

In other words, we are a resource for you.

We would love to help you. We would love to have this ongoing interaction because we think we can help you make better decisions.

DR. AYRES: Yeah, in the case of the clear rule, I'm not so sure. The main thing is the more we come to you, the more we delay.

CHAIRMAN CERQUEIRA: I would disagree with that, Bob. I think, you know, this is the -- you don't have physicians or medical physicists, practicing medical physicists usually within the NRC and the role of this committee is to provide input on those particular issues. And by not coming to the committee with three of these, you know, I think, issues, is, you know, minimizing the value of the committee and I think it's also compromising you know, delivery of patient care.

Radiation safety is the issue but within the context of the practice of medicine and so, you know, you bring it to us now, but I think it would have been more useful to have gotten input at an earlier stage in this. You may have still come to the same conclusion but you would at least had input from the committee.

DR. AYRES: Well, now is a great time because if you want to get more involved in the routine staff technical assistants request, there's going to be a position open very soon. I would encourage any of you

to apply.

(Laughter)

CHAIRMAN CERQUEIRA: Well, no, no, we have always wanted to get involved and inevitably we sort of get problems that come up but we would rather be proactive than just trying to react to things. Now, wait a minute, Donna-Beth Howe wanted to make a clarification about --

DR. HOWE: I just wanted to clarify the public availability. When the NRC headquarters responds to a regional TAR, that's not publicly available but routinely the region will write a letter back to the licensee and explain why their exemption, which is -- the licensing is publicly available. So the licensee's request to the NRC for an exemption is publicly available because it's part of the licensing docket file. The region's response back to the licensee is also publicly available through the ADAMS system. So there is public availability of the information, not specifically are TAR response back to the region, but the end result and I just wanted to make that clear.

I also want to make another point clear is that if we do go back to the ACMUI as a whole committee, we have to publicly notice. So you just want to keep that in mind, but if it's subcommittee, then --

CHAIRMAN CERQUEIRA: I think it's individuals. I think to talk to the medical physicists and the radiation oncologist and the cardiologists would be an appropriate thing to do. All right, Charlie, do you want to make --

DR. MILLER: Can I make a proposal?

CHAIRMAN CERQUEIRA: Yes.

DR. MILLER: We have a gentleman here who wanted to finish his statement but since we're a little bit ahead of schedule, I'd like to propose for a few minutes when we're finished with this, that I can engage the committee in some dialogue on what we're talking about here, aside from specific cases, but maybe more in process.

CHAIRMAN CERQUEIRA: Okay, that would be appropriate.

CHAIRMAN CERQUEIRA: Okay.

DR. TRIPURANENI: Essentially, I want to clarify, Mr. Chairman, your comments about the second X-y-z coordinates and as Dr. Ayes pointed out, I think it's a lot more than just setting up x-rays coordinates. Various oncologists have taken the responsibility and once again, to reiterate ASTRO's position, we feel that both the authorized user and authorized medical physicists be present, both of them be for the gamma

knife radiosurgery and obviously there are extenuating circumstances and occasion exemptions that could be granted but not the one that has been granted in our judgment is the right one. Thank you for this time.

CHAIRMAN CERQUEIRA: Thank you very much. Great. All right, so Charlie, do you want to get a microphone and --

DR. MILLER: Yes. You know, quite frankly, a lot of what I heard disturbs me as a regulator. I've spent the bulk of my career on the reactor side of the house and the way the licensees are engaged on the reactor side of the house, the dialogue that takes place back and forth when we would entertain proposals for changes to licenses or license amendments or exemptions or anything like that, is much different than what's done here with regard to medical applications.

We're, you know, in a sense, dealing with nuclear materials in general. I'd like the opportunity to spend some time engaging my staff on some history on why we do business as we do and maybe get back to the committee with regard to some thoughts that we might generate. But that said, I think that a lot of the concerns raised today are fair concerns. I mean, patient care is, of course, very important and I don't want anyone to walk out of the room to think that NRC is

slipping about that. I don't think whatsoever Dr. Ayres was implying that.

Our regulations are set up to protect public health and safety and recognize that the NRC is not in business to get into physician's areas of expertise but we are in business and we have a statutory authority to protect public health and safety from radiation and that's what we really need to focus on as you've tried to remind us from time to time during this presentation.

But part of what we have to do and what I have to do as a manager is, we have limited resources to do the job which we have to do and one of the things that we strive for, whether it's in reactors or whether it's in materials use, including medical use, is that we need to have people who are applying to us for licenses or changes to licenses or exemptions to licenses to submit quality applications to do so. And if the applications are not quality applications, we're faced with one of two things. We either reject them based upon the lack of merit, which I think has probably been the history here, or we have to engage them to try to improve that and we have to make a value judgment as to whether or not we would, you know, spend the resources to engage them or lob it back into their court so that they submit something back, but in fairness to them, they need to

know some parameters of what latitude that they really have to engage us and that's where I would like to engage my staff on how we go about doing that and maybe improve the process.

The second part of what I wanted to say relates to the use of the committee to help us. You're an advisory committee to us. We have timeliness goals that we have to meet with regard to dealing with applications and given the fact that the committee meets twice a year, we would need to find an alternative means. I don't think it does anyone any justice for us to present cases to the committee that we've already past judgment on and then have the committee either criticize or endorse the judgments that we've made. It would far better serve everyone, including the public, if we could get the benefit of your wisdom prior to us making the decisions and I think we would probably have to search for a mechanism to be able to do that.

Whether that's to seek counsel from individual members of the committee as we're dealing with an application and -- or how we would engage the committee as a whole and I think that's probably worth some thought on all our parts.

CHAIRMAN CERQUEIRA: I think it would be important to pursue that. You know, and again, the

committee a large composition, which was intentional and some of us have, you know, our own little areas of interest and -- but I think if something comes up, contacting the appropriate committee members to get a balanced viewpoint would be the best way to serve the NRC and serve the public. And I think you're right, once the decision has been made, I'm not exactly -- you know, all we can do is either agree or criticize and the decision has already been made, so it is a futile exercise and I think engaging members up front would be the ideal -- Ralph?

MR. LIETO: Yeah, I want to follow up on something that Dr. Brinker asked a few moments ago and thank Donna-Beth for the information on the ADAMS, because I think it might be helpful if there was some -- and I'm making this suggestion -- if there could be some means that as these requests are acted on, that either in your quarter or your bi-monthly newsletter, you know, some brief reference to it or something like that, because in the methodology that's been described, unless you knew that the, you know, exemption had been granted or denied, and what the specific licensee was, or who that specific licensee was, you wouldn't be able to find that information, you know, looking for it. And I think if people were denied exemptions and the reasoning why,

that if there were some valid reasons where an exemption might be appropriate and a licensee could meet those criteria for reasons why the judgment was denied, then I think, you know, that it has a lot of benefit and I know the resources are limited, but if there would be some way that actions were documented and the licensee would go to that reference via, you know, something on a website or your newsletter or something of that nature, I'm sure you probably have maybe the best way to consider that. I'd just like to leave that as a suggestion to the NRC staff, because I think as Dr. Brinker pointed out, you know, you don't know why or the fact that you could even apply for an exemption meeting certain criteria, you know, people aren't going to do it.

CHAIRMAN CERQUEIRA: David, Ruth and --

DR. DIAMOND: So, for example, Charlie and Tom, in those unusual cases where there may be some questions regarding an exemption, my simplest response or advice would be have a member of the staff pick up the phone, call one of us, "David, you did these gamma knives, do you think it is -- how long do you think it would take you to respond? Do you think 50 feet is too far away, 100 feet"? Just giving that simple practitioner information may be the easiest way to go.

We're not telling you how to make a

decision; we're providing some technical advice or some practitioner advice and again, that is the most real time way that we can be of help and I'm sure all of us would be more than happy to help you on an intermittent basis.

CHAIRMAN CERQUEIRA: Right, and again, some of these things, I mean, I'm a physician. I don't understand what some of these things are. And for those of you that aren't, you know, in hospitals all the time, you have no idea the context in which this is being done and getting input from committee members and you know, as Chair, I would be, you know, happy to make sure that you get a mixed -- that you get sort of a balanced input into the issue. And I think that would be important, but take advantage of us. And as David said, if we're too busy, we can tell you but some of these issues, you know, in a relatively short time, I think we could give you appropriate insight to help you come to a decision which would both be, you know, safe for the users but at the same time facilitate medical care.

Did you want to make a comment?

MS. McBURNEY: Yeah, just to let you know how we handle exemption requests of this nature; usually if it needs more clarification, we will write them back and ask for more detailed information before we just say yes or no. And also, we do utilize members of our -- we

have a radiation advisory board that covers more than just medical but we're likely to call up one of the medical members if it's a medical issue to ask their advice on a particular exemption request or if there's a particular contentious licensing issue, so -- and fax them the detailed information if we need to, to get that information.

DR. BRINKER: So what kind of -- have you had a situation where you've granted exceptions in situations like this and what kind of direction would you get in your situation from actions that the NRC, for instance took? If you knew that they rejected all these applicants, would you independently -- still feel independently --

MS. McBURNEY: We would take that into account as to how they handled that. I mean, and we read up on how other states also are doing treating those situations, but for the most part, we -- you know, we have a little bit different rules and so first of all, we have to base it on what our rules say and then go for, you know, what we believe is still protected by public --

DR. BRINKER: And Dr. Miller, is there a mechanism where you're aware of exceptions to rules that the states can grant in a state that's not an NRC state and would that be looked at or considered when

adjudicating a single request from an NRC licensee? I mean, we have two different systems and it seems to me that we have possibly a difference in the way patients can be treated depending upon what state they're in and I just want to know whether there's a reason to coordinate that.

DR. MILLER: Well, I mean, there's certainly reason to coordinate where it's at all possible and I would have to defer to some of my staff in other specifics, who have been dealing with this area for more than the two months that I've been in this job. But, I don't think we have systems that are completely independent of each other. I don't want to give that impression. I mean, the states have been -- those that are agreement states have been delegated the authority by the NRC to conduct their own programs. However, periodically, the NRC does evaluate state programs to make sure that the programs are consistent and meeting the intent of what we would want. And I think what you're asking for, Dr. Brinker, is are we available of all of the information and data that's out there so that we have the benefit of previous decisions that are made when each of us make decisions and you know, I'd have to defer to Tom or some of the staff on how we go about doing that. I'm not aware that we have a data base that

does that.

MR. ESSIG: I'm not aware of a data base that --

CHAIRMAN CERQUEIRA: I don't think it exists and certainly with the training and experience that's one issue but there is so much variability but Niki, you've been patiently waiting.

MS. HOBSON: Well, I really appreciate Dr. Miller's comment about that if NRC receives quality applications for exemptions it's easier for you to deal with them. And I just wondered, do guidelines exist or could they be produced that would advise licensees what you expect to see in an application for exemption?

And my second point is, if not, it seems like that that would be a logical thing to do is develop some guidelines so everyone knows, you know, what's expected. And my second comment is that, you know, a person's life is at stake in many of these cases, maybe even most of these cases and for NRC staff to take one extra step to try to figure out a way that this patient can get the care that their physician thinks they need is not really asking too much.

DR. MILLER: Thank you.

CHAIRMAN CERQUEIRA: Leon.

DR. MALMUD: I would also like to address

Dr. Miller's comment. There have been issues raised in the last day and a half before this committee for which I am unprepared to offer advice because I'm not knowledgeable in that specific area. I am also aware that there are members of this committee who are knowledgeable about the respective areas and your suggestion that they be brought into or we be brought into the process early on, I think, is extremely constructive and would allay a lot of the concerns that we have about how decisions are made now.

The other element that I've witnessed is that sometimes people presenting issues to us say, "We didn't make the decision, we were not part of the process, don't shoot the messenger". That is of no value to us whatsoever. We have no idea why the decision was made and the messenger who delivers the message basically says, "I don't know why it was mad either, don't ask me". That is extremely unconstructive. So I would like us never to have that experience again and that when someone is sent to speak to this committee, that that person be adequately prepared to speak to the committee or uninvited to speak to the committee and under no circumstances should we be given information for which we have no background personally and for which there is no data base.

Now, with respect to a specific issue, this issue of the two rooms for gamma knife radiosurgery, that is a new situation which has never been presented to the NRC before, I assume. It's a whole new set of circumstances. And that would be the kind of a circumstance in which an exemption might be granted because it's a new circumstance, it's not something that occurred before which is, I think, the issue that you were raising, Jeff, if I'm correct.

To say no without having asked any radiotherapists who are serving as consultants on this committee, for their advice, I think is too quick a decision and may be an incorrect decision, although I didn't see any data that indicated it was incorrect. I also am not sure that even among radiotherapists there would be any consensus with respect to the number of staff but it certainly would be valuable to ask them up front and I think any members of this committee are available in most situations via phone call from the Chair to respond to specific questions.

So I think that your suggestion, Dr. Miller, is one of the most constructive that we've heard in the day and a half that we've been here and I think would allay a lot of the anxieties and misgivings that individual members of the committee may have. Thank you.

DR. MILLER: Message received. But I would like to say just one thing with regard to exemptions. I think we all have to caution ourself. If it's a rare and different kind of occurrence that warrants an exemption, I think it needs to be considered on its merits. If we find ourselves issuing exemptions over and over for the same kinds of thing, then there is something wrong with the regulations that needs attention because we shouldn't be regulating by exemption.

DR. MALMUD: I fully agree and the other issue that I didn't mention about the exemption is there are certain situations in which the exemption is, in a sense, an emergency because of a clinical need. There are others in which the exemptions being asked for in the planning process. Obviously, the first decision may warrant an exemption. The second one may warrant consideration rather than a simple decision that would prevent or encourage someone to pursue something.

DR. MILLER: Yeah, and I do -- you know, with regards to the staff, I've got to defend them some because we have people here who are very dedicated to this and I think what we have to work at is communications is a key tool and how can we better communicate with the committee so that you can serve us the best and you can give us the advice that we need to

do our job but at the same time, you're much less frustrated with regard to, you know, how we interact and how we provide information back and forth.

DR. MALMUD: If I may, the other comment that I would make is that most of us -- well, looking at us, all of us, have had years of experience and we understand -- we understand full well that an exemption for an individual who we believe is extraordinarily meritorious, it's precedent-making perhaps and therefore, that exemption has to be made with the understanding that we're not making it for an individual. We may be setting a new precedent in which case we may be opening Pandora's box in which case we will have abrogated our responsibility for public health and safety.

So I think we're all fully aware of that and we understand the risks. Health care is a field in which the public is very concerned about errors and we don't want to compound any of those errors.

DR. MILLER: Thank you. I think your comments, Doctor, are very well timed and very well said and I agree with everything that you've said.

CHAIRMAN CERQUEIRA: One last comment from Tom and then we'll break.

MR. ESSIG: I just wanted to add to what Charlie Miller was saying regarding the process that we

use here at headquarters. We have a technical assistants review process which sometimes we get caught up in the need for timeliness, support -- timely support of our regions who are doing the licensing actions and in all the cases that we've cited here, it was a region-based licensing action. At the headquarters level, we only do two kinds of licensing actions, sealed source and device reviews, and exempt licensing distributions. And so we are, in this case actually consultants to the regions and so they have certain time limits goals for their licensing actions. We try to be supportive of them and so what we try to do is to then balance the quality of the review with the timeliness of the review and arguably in some cases like we've talked about here today, it probably would have behooved us to consider consulting with individual members of this committee and so I'm taking back as an action to certainly factor that into the process because what we're talking about there in this Technical Assistant Review is simply a process and it's not bound by regulations. It's just an administrative process that we use here at headquarters.

MS. McBURNEY: Tom, are they precluded from -- are the licensing people in the regions precluded from interacting directly with a member of the advisory committee? Would that have to go through headquarters?

MR. ESSIG: Oh, I don't think they're precluded, no. They would probably always --

MS. McBURNEY: I was just thinking of cutting down on the time frame.

MR. ESSIG: Yeah, just the general organizational hierarchy, they would probably usually defer to us but I don't know that they're precluded from doing that.

CHAIRMAN CERQUEIRA: We'll take a break and reconvene. Thank you. This was very helpful.

(A brief recess was taken.)

CHAIRMAN CERQUEIRA: If we could -- Tom, we had a question about the -- at 3:15, the subcommittee working meeting; is that -- that's an open meeting?

MR. ESSIG: Yes.

CHAIRMAN CERQUEIRA: Okay. Okay, the first item is the discussion, "The Listing of Certain Practitioners in 35.1000", and Leon is going to be presenting the material.

DR. MALMUD: Thank you. It has been brought to my attention that perhaps unintentionally the group of medical practitioners with the greatest experience in administering intravenous radiopharmaceuticals has been excluded from the practical application of one mode of therapy. The issue has to do with TheraSpheres. Nuclear

physicians dating back to 1970 were administering microspheres intravenously for lung perfusion scanning, human microspheres. Those were particles which were smaller than 20 microns administered intravenously which embolize into the lungs occluding a very small percentage of the vasculature in the lungs and giving an image of the profusion pattern within the lungs in order to rule out a diagnosis of pulmonary embolism.

The product at that time were known as 3M microspheres or HAM, H-A-M for human albumin microspheres the two products coming up with the two different names from two different sources. And they were used for a number of years for lung profusion. When TheraSpheres came along, because they were introduced by the manufacturer through the methodology of being not a radiopharmaceutical, but basically a mechanical kind of operation, they went under Category 1000 rather than 1, 2 or 3, 400. When apparently when the modality was reviewed by the NRC, it accepted the fact that the work which was done in Canada and which had been presented for approval, not used in the radiopharmaceutical approach was, in fact, a -- not a radiopharmaceutical and therefore, would be more appropriately listed as a form of therapy.

To make a long story short, what's happened

is that now individual hospitals which are approached by the manufacturer for introduction of this new therapy to the care of patients see this as a radiotherapy technique rather than a nuclear medicine technique. There are hospitals, of course, which have radiology and nuclear medicine sections or departments but do not have radiotherapy departments. This has created some turf battles within and among the specialists; radiotherapists, nuclear physicians, nuclear radiologists and in theory one could also see being brought into the desire to practice using TheraSpheres other specialists such as interventional radiologists who may want to administer these materials intra-arterially but would have to do so in conjunction with someone who is also an authorized user, a medical oncologist who would similarly want to and have access to administering there TheraSpheres in conjunction with an authorized user.

The basic issue is that unintentionally the group of physicians with the greatest experience in administering radiopharmaceuticals has been excluded from easily accessing and administering this radiopharmaceutical and other radiopharmaceuticals that are currently in the pipeline and will be approved if we follow the guidelines that were used here. Now, how did this happen? And the answer is we don't know with

certainty. We do know that the manufacturer went through the non-pharmaceutical approach and that's clearly how the NRC approached this because it was presented to them in this manner.

But it would be very useful if the NRC would look at in the future applications looking not only at the radiation issue involved but also the clinical expertise required to administer the product or use the product and to look at it with a wider range of interest than simply trying to classify it in one group or another.

The immediate problem is that the yttrium-labeled microspheres are not readily accessible to nuclear physicians. This would require for those with broad licenses an amendment to their license and for those who do not have broad license, an application process. This will slow down the delivery of this new form of therapy to patients who otherwise would be able to receive them rapidly because there are more hospitals with radiology and nuclear medicine departments than there are hospitals who have radiotherapy departments.

I am not presenting any argument which is adverse to radiotherapists, medical oncologists, interventional radiologists from using the material. I'm simply presenting the concern of those who have been

excluded unintentionally from easily accessing and using this modality. And I would like the wisdom of the committee and the NRC in dealing with this.

CHAIRMAN CERQUEIRA: Richard and then Subir.

DR. VETTER: I think it's incorrect that broad licenses have to amend their license. I think they have the authority to determine who may administer the material. Specific licenses, however, do have to go in for an amendment.

DR. MALMUD: Thank you.\

CHAIRMAN CERQUEIRA: Subir?

DR. NAG: Yeah, I think the whole treatment of TheraSphere is a complex treatment requiring multiple disciplines. I'm not going to say who should be doing it but I'm just going to outline the various steps. One will be a distribution study which, you know, is normally done by nuclear medicine to see where the dye is going, not the material but where the radio labeled isotope is going. The second part is the introduction of a catheter to the site and normally that is done by an interventional radiologist to make sure that the catheter goes to that site although that could be done by a surgeon.

The third part is a knowledge of the tumors. It is not enough just to give somebody radioactive

material, but to know how the tumor would behave, how much radiation those tumors need, what the dosimetry is, that's the third component.

And the fourth component is a mixing or dilution or receiving of the radioactive material. The reason why I'm separating that is that in some institutions the encapsulated material are received in a separate department. The non-encapsulated materials are received in a separate department. And the fifth one what we are discussing the actual introduction of the radioactive material. So you have to have the five components at best.

For example, who is doing which component of that, you know, that may be up to the institution but you have to have each of those five at best.

CHAIRMAN CERQUEIRA: Again, just one comment, I mean, we're talking here about physicians. We're talking about people who have gone through four years of university, four years of medical school, you know, many nuclear medicine physicians have had, you know, several years of nuclear medicine, internal medicine and then they've had, you know, extensive time periods and so you know, we've got people who have got a very good knowledge base including aspect of radiation safety and this issue came up with the neurosurgeon, it

comes up with a cardiologist. And there are unique things about the radiation but how much of that is unique for a radiation oncologist versus how much of it can actually, you know, be part of medical knowledge, or can be, you know, learned by specific people. How much training and experience is required for that? And so, you know, Charlie, this committee to some extent in the past has kind of been the battleground amongst the various interest groups within medicine for dealing with some of these issues.

And I think this is, again, another issue that sort of comes up. So that's just sort of a general comment, and we'll go to Doug and then Ruth.

DR. EGGLI: I think because of a strategic marketing decision, a material which is far much more like a radiopharmaceutical than a brachytherapy device was classified as a brachytherapy device for strategic marketing reasons and licensing reasons and not for medical reasons. In fact, this is very much like the particulate materials used all the time in nuclear medicine and nuclear medicine physicians are very comfortable with the knowledge of the tumors with the managing of the therapy. I do complex dosimetry in my practice on a weekly basis. So that I think there need to be a wide range of options for physicians who are both

trained and knowledgeable in the use of materials but have come to this by different certification pathways to have access. And if we look at something like these materials as Dr. Malmud said, they will be used in a wide variety of clinical settings and we run the risk of depriving people of therapies which may be useful because of a fluke of licensing of a material.

There are far fewer broad licenses out there than there are specific licenses. So in my own hospital our Radiation Safety Committee may be able to define who the authorized users can be but in the vast majority of licensees out there, that's not going to be the case. And again, it would be shame to see a class of well-qualified physicians excluded from offering a valuable therapy by simply a strategic marketing decision made by a corporation in the licensing process.

CHAIRMAN CERQUEIRA: So, Doug, you're supporting the fact that nuclear medicine physicians as a result of their training and experience, should be allowed to do this, that there's no additional risk; is that -- how -- within sort of the rule space that these guys operate in, how should they do that?

DR. EGGLI: That's not less clear to me. One option is, obviously, rulemaking. The other option is exemption based on training and making an exemption

rather -- training and experience, rather broad based. I realize exemption should be an occasional thing, but in this case, we have a rule which is not -- doesn't completely serve the needs of the regulated community and since we're still in the rulemaking process, it might be appropriate to address it from -- in rulemaking space rather than as exemptions, because I think you will be pummeled with requests for exemptions.

CHAIRMAN CERQUEIRA: Ruth?

MS. McBURNEY: We'll get more into this afternoon in the subcommittee on training and experience for these different modalities but in preparation for that, I did check with several states to see how they are treating the licensing of the microspheres and in some of the states they are allowing the physicians that are trained and experienced in unsealed byproduct material used for therapy, due to the delivery system and the potential for contamination and in other states, they're treating it as brachytherapy due to its classification as a sealed source. So there is some variation out there right now in what's being allowed.

AUDIENCE MEMBER: So what do you recommend for who should be doing this?

MS. McBURNEY: I think that either could do it because of the training and the experience.

CHAIRMAN CERQUEIRA: David, what are your thoughts on this?

DR. DIAMOND: From a pragmatic point of view, take an individual like Dr. Eggli here, who may not have a -- do you have a broad scope?

DR. EGGLI: Yes.

DR. DIAMOND: I'm sorry. What will happen pragmatically is that if this is, if this is interpreted in such a way that only radiation oncologists can do it according to Subpart K35.1000, the NRC will be flooded by exemptions, by well-qualified individuals, people who have lab experience in similar materials and this will be an example where I think that there is very little rational basis for segregating the use of this material based upon the nuclear medicine physician, radiation oncologist, and so forth, provided they have the appropriate background.

In our particular center, we deliver all of the therapeutic radio nuclides. We have a wonderful relationship with our nuclear medicine colleagues who do the dosimetry work and obviously, these patients tend to be controlled by the medical oncologists because they tend to have obviously, malignancies that are amenable to medical oncology therapies. That's how we do it at our center.

We recognize that that may not be possible or optimal in other places and this would be an example where I would agree with Doug and I would agree with Leon, that provided those other individuals, meaning those individuals from the nuclear medicine specialties, disciplines, would be appropriate to utilize these modalities.

CHAIRMAN CERQUEIRA: Thank you, David. Ralph, do you have a comment?

MR. LIETO: Well, I just had a question, you know, for NRC staff. Are the microspheres do they meet the NRC definition for a sealed source? Is that true?

MR. ESSIG: I'm going to have to -- Donna-Beth is nodding yes.

MR. LIETO: I mean, I understand they're in the sealed source registry but isn't there specific criteria that a sealed source has to meet in order to be classified as a sealed source and do these microsphere meet it?

DR. HOWE: They are sealed sources. The yttrium is embedded in a glass matrix. The material does not migrate outside of the glass matrix. Source spheres is an ionic sphere. The yttrium is firmly bound to the ionic sphere. So they are sealed sources. They may not look like your typical sealed source that's included in

a metallic capsule but they're just teeny, tiny little sealed sources.

CHAIRMAN CERQUEIRA: So I guess that restricts what can be done. Now, Jeff, we'll need an authorized medical physicist there, is that what you're going to say?

DR. WILLIAMSON: No, no. Can I ask a question of the staff for clarification?

CHAIRMAN CERQUEIRA: Sure.

DR. WILLIAMSON: Okay, so this is an SSDR device. How much latitude do you have within the guidance space, within 35.1000, to allow 35.300 as well as 400 authorized users to prescribe the material?

MR. ESSIG: I'm going to have to defer to my staff on that one because of my newness to the topic myself.

CHAIRMAN CERQUEIRA: Why don't you each take a seat outside?

DR. WILLIAMSON: I want to understand the administrative and regulatory problem a little better.

CHAIRMAN CERQUEIRA: Yes, I think that would be helpful for everyone because, you know, the general feeling seems to be they should be able to do it.

DR. HOWE: Actually, as part of my talk this afternoon in going through how we developed the guidance

for -- first of all, how we decided which things would to into 1000 and then how we developed the guidance for each one of the uses we have. The question is --

DR. WILLIAMSON: The question is, for an SSDR classified device, a brachytherapy source, if you will, a very unusual one having said that, do you have the latitude to allow in your guidance if you wanted to, the 35.300 authorized users to prescribe this material?

DR. HOWE: I think one of the things we have to consider is that for a long time we didn't have a lot of really new products coming down and now we're --

DR. WILLIAMSON: I really was asking a strictly --

DR. HOWE: No, no, but let me say that we are now seeing new products that look like they can cross boundaries.

DR. WILLIAMSON: Yes.

DR. HOWE: 35.1000 says this is a new product that may cross boundaries and we get to look at and see what we think is the best mix from what we currently have for regulations for that. So we are not restricted necessarily on 300 or 400 and we can --

DR. WILLIAMSON: Good, that was just my question.

DR. HOWE: -- we can tailor something to

meet?

DR. NAG: Can you add both? Can you say, you know, people who are qualified under 300 or 400 then use this?

DR. HOWE: We have that flexibility.

DR. NAG: And then the problem is solved.

CHAIRMAN CERQUEIRA: Dick?

DR. VETTER: I think reading between the lines, Dr. Malmud said that the needs of the patient come first and in some small institutions the only way those needs can be met is if nuclear medicine is allowed to administer the material and, in fact, he made the case, and I agree, that they are qualified to do so, especially those who are trained in and routinely administer therapeutic radiopharmaceuticals.

DR. HOWE: I will say that when we were developing the guidance we considered this to be a brachytherapy source, a permanent implant brachytherapy source and we looked to see who had the training and experience to use permanent implant brachytherapy sources and what training they had to adequately describe the dose and do the calibrations and things like that and we came to the conclusion that the 400 physician had that training and we were not as comfortable with -- we certainly were not comfortable with the 300 physician

with 80 hours of I-131 or P-32 training or the diagnostic nuclear medicine that does not routinely use therapy treatments.

CHAIRMAN CERQUEIRA: Jeff, Doug and Leon, maybe you could respond to that? I mean, does a 300, you know, I-131 therapy doc have the appropriate knowledge to --

DR. EGGLI: I think in general, the answer to that is yes. Again, there are 300 issues that clearly apply to this material that don't apply to 400 issues which are the contamination risks. There are significant -- this behaves like any particle that I inject. I put particles into joints. I put particles into the interstitium. I put particles everywhere that are therapeutic in nature and there are contamination issues in the administration of these particles that are non-trivial, particularly with high energy beta emitters. These are non-trivial issues and they behave functionally, like a 300 category therapeutic agent and they really -- other than the fact that they don't leave the tissue and I actually in 200 I have radiopharmaceuticals that never leave the tissue, but they're diagnostic rather than therapeutic.

But other than the fact that they're there in the tissue permanently, these for all other practical

purposes behave like agents which are governed in the 300 section, not like agents governed in 400. Now, I'm not suggesting that physicians who are certified for 400 should be excluded from their use. But I'm saying their primary behavior with one exception which is longevity, are 400 and again, I can calculate how long they're going to live in the tissue as well as someone trained in 400.

DR. HOWE: Well, I think one of the things we're also seeing is initially when the products were coming through the PMA process or the HDE process, which is the humanitarian device exemption process, they were presented with very clear amounts activities unit doses almost, and what we're seeing now that they're getting out into the medical community, is that there's a lot more decision making based on how the patient has been treated and what the radiation dose they can accept in certain parts of the liver and we're not seeing whole liver. We're seeing really a lot of things that I would probably characterize more as radiation oncology decisions.

DR. EGGLI: Well, those are the decisions that I make in therapies every day. And as far as the tools from which those decisions are going to be made, fall into the 200 range which are going to be profusion studies looking at the distribution and the techniques

are going to be done on my computers, which are going to determine the dosimetry in large part. So that these kinds of decisions are the kinds of things that people who are authorized in the 300 range do routinely. And so that, yes, calculating those kinds of doses are things we do.

We do far more complex dosimeter than this with our high does radio-iodine therapies every day.

DR. HOWE: But I think you also need to keep in mind the difference between a therapy at a broad scope and a therapy at a limited specific. So when you're speaking, make sure you're speaking for both groups.

DR. EGGLI: I understand.

CHAIRMAN CERQUEIRA: Okay, just one comment. I mean, would you restrict -- I'm board certified in nuclear medicine, so --

DR. EGGLI: But are you approved for 300 use?

CHAIRMAN CERQUEIRA: Yes, for I-131 therapy.

DR. NAG: Would you be comfortable in doing an implant in a liver, injecting --

CHAIRMAN CERQUEIRA: No, no, but, you know, so do we need some restrictions on --

DR. EGGLI: I guess the answer would be that I think people have to determine what they're comfortable

doing and there are liability issues that I certainly wouldn't do a procedure that I wasn't comfortable with and familiar with because I think I have a horrible liability.

CHAIRMAN CERQUEIRA: But that's their role is to, you know, you trust the judgment of physicians but they do make errors and they need to prevent that. Ralph.

MR. LIETO: I was going to say historically the NRC has always had 300 out there and limited specific physicians to just say I-131 use, okay, and precluded them from other types of 300 authorizations. So I don't think that that needs to be a situation that we need to be using to maybe preclude this going into 300. You know, I don't know if we need a motion at this time or if this is going to be addressed later on, but I think that these approved uses of the TheraSpheres and the Zevlin should be approved and put into the regulatory space under 300, because we're talking about unsealed uses and you know, microspheres have been considered unsealed uses, you know, for almost 30 years, okay, and as Dr. Malmud pointed out earlier. So I don't think that the NRC is doing anything in terms of particle size and authorization for use that they've not allowed in the past.

DR. HOWE: I would like to see you decouple Zevlin from the TheraSpheres because Zevlin is a radiopharmaceutical and we looked at Zevlin and we looked at our current regulations and we looked at our requirements under 300 and we said, there is no reason for Zevlin not to be 300.

MR. LIETO: Right, well, what I'm saying is they both should be put into 300 space. So, I mean it's --

CHAIRMAN CERQUEIRA: Is that a motion you're making?

MR. LIETO: I'm going to make a motion and you can discuss it.

DR. HOWE: One's already there.

MR. LIETO: I'd so move. I think it's too early.

CHAIRMAN CERQUEIRA: Too early? All right, so a little bit more discussion. Jeff?

DR. WILLIAMSON: Well, several points; I mean, a general point first of all that's more appropriate for this afternoon, but I think we have two extreme cases before us that really will help us, I think, set down some precedents for the way we think about this. We have the GliaSite, which is using a nuclear medicine source, essentially in a brachytherapy

delivery mode, which, you know, from my perspective as clinical physicist, involved not only a sealed source, but confined radioactivity that is surgically positioned by a radiation oncologist. It involves some element of surgical skill and localization. And on this other end of the spectrum we're talking about now, we have something that is a brachytherapy source but the treatment -- delivery and treatment planning technology, you know, really is a nuclear medicine base and different than the paradigm we use in radiation oncology commonly.

DR. HOWE: I think what I'd like to see is I'd like to see the working group that you have on the emerging technology work closely with the staff so that you can really understand where we're coming from and we can understand where you're coming from and reach a ground that we'll feel comfortable with.

DR. WILLIAMSON: I think that's probably important. I mean, you know, what the -- I'm not sure we're talking about -- the second point is, is, you know, if you look at, you know, radiation oncologists versus a 300 practitioner, you know, a radiation oncologist I think certainly has a more vast and focused post-graduate education on oncology in general. And so, you know, the big issue is, is one issue is how important is that to this device, to use it safely? We did make a decision

early on in the formulation of the revised Part 35 that in higher risk modalities, you know, the clinical expertise could not be decoupled from the issue of using it safely because the issue of prescribing it in the -- to the correct -- you know, the issues of patient selection and dosing simply could not be decoupled -- are not safety issues. Well, they are safety issues if one treats the wrong population, the patient. So, you know, that has to be borne in mind as well.

And I guess the third issue as I look at 35.390, it doesn't say 80 hours here, it says 700 hours.

DR. HOWE: We have a new requirement, a new regulation now. When we were first looking at it, most of your 300 was an 80-hour. I can see moving to a compromise where we insure that the users have the right training and experience to cover the issues we're concerned about radiation safety.

DR. WILLIAMSON: Well, I think, this is a technical question, then, too. As I understand I-131 therapy requires the 80 hours of didactic training and experience but the unrestricted right to prescribe any radiopharmaceutical I thought as the regulation is now written and promulgated through the land requires a 700-hour training. Is that not correct?

DR. HOWE: That's correct, but we still have

Subpart J which is only 80 hours and so you can go either route.

DR. WILLIAMSON: Okay, I think one compromise might be to place a restriction on the use of Subpart J for this purpose.

CHAIRMAN CERQUEIRA: Yeah, I think that might be appropriate. Subir?

DR. NAG: We are going to have a -- I think this is somewhat premature because we were going to be having this discussion later this afternoon. We haven't had a chance to bring up all of this issue and so we are bringing up a -- before the whole committee before the subcommittee has had a chance to work it out. You know, we may come up with some suggestions. Like I said, there are five different components to this. Can one person do all the five components or should we make it the responsibility of a group of individuals that can make sure that all the five components are taken care of? We haven't had a chance to discuss all this. I think some of these issues, fine, we have brought it up, but I don't thing we can solve it. I suggest we table it until we have had a discussion.

CHAIRMAN CERQUEIRA: I think we will discuss it later on. It may be premature for a motion, but I know some of the people have flights that may preclude

them from being involved in all the discussions. It would be nice to get their input. Dick, I mean, I know you have a flight. What are your thoughts on --

DR. VETTER: Well, I agree entirely with Dr. Malmud. I don't think we should be restricting this to either therapy or nuclear medicine. It really depends on the institution and the capabilities of the physicians there. The materials certainly does behave like a radiopharmaceutical and all of those points have been well-made. Incidentally, there is a diagnostic test that goes along with this that essentially does the same thing when the microspheres are administered. They have to determine the distribution of particles in the liver prior to administration of the microspheres and that's done by nuclear medicine.

CHAIRMAN CERQUEIRA: Is there anybody else who's not going to be here for this afternoon's session that --

DR. MALMUD: I will not be here this afternoon and Dr. Nag, the reason that this is being presented this morning rather than this afternoon because it was originally on this afternoon's agenda, was that I have a conflict this afternoon with the Armed Forces where I must be. So that I'll take the blame for that. The Chairman had laid out the program more efficiently.

The --

CHAIRMAN CERQUEIRA: I didn't realize I did it.

DR. MALMUD: The issue -- or he'll take credit for having done it. The issue which is the one that I wanted to get on the table is that it might be helpful in the future in dealing with new devices because there will be very innovative things coming down the pipeline, to look not only at the existing regulations but the history of the specialties and how they have provided services similar to these new technologies in trying to come up with proposals that would deal with how the new techniques would be employed.

With respect to this specific one, what I would like the staff to consider is how we can deal with the accessibility of the TheraSpheres to the nuclear medicine community without flooding the NRC with unnecessary applications from people who are already fully certified and competent. That's the last thing that we want to do to the NRC is to see I think there's 6,000 providers putting in amendments to their license so that nuclear physicians can have direct access.

DR. HOWE: And the point I wanted to make is that the 35.1000 guidance is up on the website. We don't have to go through rulemaking. We can reach a consensus.

We can modify the website as needed. We now have a working group that we can interact with. We did not have that before and so I think if groups work closely together we can come up with a mutually acceptable guidance.

CHAIRMAN CERQUEIRA: I agree with that and I'll follow Dr. Nag's suggestion and move on but before we do that, we have two people to the back microphone who I think would like to make comments. Mr. Uffelman?

MR. UFFELMAN: Bill Uffelman, Society of Nuclear Medicine and I want to you know, along with Donna-Beth, the contemplation of the Society when we got into this issue was that we were talking about the 35.390 physicians, not the 35.392's and `94's. And we knew that when Subpart J was added we kind of had these 80-hour wonders, I mean, not to speak ill of them, but we had this notion that there was this dichotomy created when the old rule was carried forward for awhile and it has never been contemplated in my office at the Society of Nuclear Medicine that the people who were only trained for 80 hours in iodine therapies for thyroid were people who, in fact, should be using, you know, microsphere therapies with Yttrium-90. And that was, you know, that was what we were speaking to and what Dr. Malmud was, in fact, speaking to.

CHAIRMAN CERQUEIRA: Thank you, Bill. Jeff.

DR. SIEGEL: Just a quick comment; I think that the NRC was visionary in adding 35.1000 to the Part 35 rewrite and I think one of the unintended consequences, however, was that as new technologies evolve, and they sort of overlap between existing areas as in the case of Nordion's TheraSpheres and Sirtex's SIRSpheres, I can appreciate the NRC's predicament because 35.300 material refers specifically to unsealed sources and because the manufacturers took the brachytherapy sealed source non-radiopharmaceutical rap to get FDA approval quicker there's somewhat of a trap in that these being considered by NRC now to be a sealed source when in effect, from a scientific basis since you brought up Zevlin, the purpose of Zevlin is for the material to go to a tumor and remain there for the fiscal half-life, which is scientifically no different than instilling these materials.

But I can understand because of physical form and written directive this is a different physical form so I can appreciate where the NRC is coming from and now it seems as though all nuclear medicine physicians will have to via 35-12, apply for a license amendment. And I might want to add on your website, when you talk about T&E for this brachytherapy implantation modality

that AU's could only be authorized if they meet the T&E from 490 which is the 400 brachytherapy or the Subpart J 940 for two years.

So it's not clear that a nuclear medicine physician, if applying for an amendment through 35.12, according to the language of this, which is dated October 29th, 2002, would be recognized by T&E to be people likely or capable of using this modality.

And one other thing, just for completeness, in the statement here, because NUREG-1556 Volume 90 went into such detail about patient release, and the NRC has said that if you're a beta emitter which emits only Brenstralung photons sort of as a negligible external radiation hazard and in fact, the guidance document says that there's essentially no millicurie amount that is not releasable, there's a statement here that says procedures, that is in applying for a license amendment, should describe measures taken to insure that the Bremstralung emissions from each patient or human research subject permits his or her release in accordance with 10 CFR 35.75. That was an issue totally visited in NUREG-1556, Volume 9, Appendix U.

DR. HOWE: We were hearing that because some of these patients are incredibly thin so you don't have a lot of tissue and you've got contact with bone, that

you were seeing some Bremstralung that might throw you into the category where you had to make the measurements. So that was in there for a reason just to assure because of the type of patients that were being looked at, that there was not a Bremstralung problem.

DR. SIEGEL: Right, but how would you propose somebody describe this? They'd have to calculate a Bremstralung exposure rate constant and there's only one article, to my knowledge, ever written that does that. And has anybody done that calculation?

DR. HOWE: No, your option is a measurement.

MALE PARTICIPANT: Yeah, a physical measurement of exposure.

DR. HOWE: That's what we were essentially trying to get to, is that for these patients it may be in your best interest to do a physical measurement to assure you can release them.

DR. SIEGEL: So this is something different than is in the NUREG and 3575?

DR. WILLIAMSON: No, it's allowed in NUREG and 3575 to use an exposure measurement as a basis of releasing the patient either with or without, you know, biologic --

DR. SIEGEL: But it specifically says

because there is -- the exposure rate constant is essentially zero, that there's no need to measure dose rate or administered activity for that matter as a prerequisite for a release.

DR. WILLIAMSON: I think that may be a good point is the guidance might need to be amended in that respect.

DR. SIEGEL: I'm just bringing that to everybody's attention.

DR. WILLIAMSON: But from a practical perspective, I don't see there's a problem but I think the advice to do a measurement would be well-heeded.

AUDIENCE MEMBER: All right, thanks for those comments, Jeff. Donna-Beth, you understood all the references. I don't, okay, because we will bring it up again this afternoon. I think we can --

DR. HOWE: Yeah, and I'll be going through in my talk because I'm going to be talking about the 1000 and Bob's going to be talking about the IVB part of 1000. I'll give you a little bit more of a history of --

CHAIRMAN CERQUEIRA: All right, thank you very much. I think there's --

MS. WILLIAMSON: Dr. Cerqueira, the previous speaker would like to state his name for the public record.

CHAIRMAN CERQUEIRA: Okay. Dr. Siegel.

DR. SIEGEL: I'm sorry. My name is Jeff Siegel. I'm representing the Society of Nuclear Medicine and the American College of Nuclear Physicians.

CHAIRMAN CERQUEIRA: Okay, excellent. We'll go on to the next item, which is -- Leon?

DR. MALMUD: I just wanted to ask a question. As I will not be here this afternoon, is there a consensus among those present that this issue is resolvable?

CHAIRMAN CERQUEIRA: Yes, yes.

DR. MALMUD: Thank you.

CHAIRMAN CERQUEIRA: All right, Interpretation of 10 CFR 35.61(b) and Dr. Zelac will be -- 35.61(b), "A licensee may not use survey instruments if the difference between the indicated exposure rate and the calculator exposure rate is more than 20 percent". Did I read it right?

DR. ZELAC: Yes, yes, indeed you did. This is the second opportunity that I have to speak to you about a particular topic. This is also a topic that was brought to our attention by you, so I am in a sense, responding hopefully satisfactorily to a concern on this particular issue. 35.61, 35.61 deals with the calibration of survey instruments and the specific -- you

all have the handouts in your books till we get the slides up. I'm on the second slide at the moment.

The specific requirement in Section B, which I referenced, is that the use of a survey instrument is prohibited if the difference between the indicated exposure rate on the instrument and the calculated exposure rate during the calibration procedure is more than 20 percent. In other words, if the response of the instrument differs from the calculated exposure rate by more than plus or minus 20 percent, the instrument is deemed not satisfactory for use.

The next slide deals with the changes from the previous requirement. Previously there was an implication but not a clear statement that instruments which are out of calibration are not to be used.

DR. WILLIAMSON: What does "calculated exposure rate" mean?

DR. ZELAC: Calculated means that there's a source which is traceable to NIST and you, based on the activity of the source or the output of the source, know what the exposure rate at a particular distance from that source should be.

DR. WILLIAMSON: But it refers to the calibration source and not an arbitrary radiation field that you're measuring.

DR. ZELAC: Absolutely. That is absolutely correct. It refers to the calibration source. And secondly, the change from the previous requirement in Part 35 is that the acceptable response range for calibration without a correction chart or a table, has been broadened to plus or minus 20 percent. Now, guidance that went along with the previous Part 35 indicated that instruments should not be used. It was implied that instruments should not be used if they -- it was stated that instruments should not be used if they're out of calibration and the implication was that plus or minus 20 percent because that is what was referred to as acceptable in the calibration, the model calibration procedure.

Additionally, what was stated is that a correction chart or table should be utilized to account for the difference between what the exposure rate on calibration was and what the instrument indicated. The threshold for including such a chart, however, was not included.

The rationale for the requirement in the current regulation is consistency in general with the calibration acceptability in a national performance standard. As you well know, this agency and all other federal agencies is obligated to use national performance

standards when they are available and they apply to the particular activity being regulated.

In this case, we're talking about an ANSI standard N323A from 1997 and the title is here. So what we're trying to do is to reflect in the regulation the requirement -- the suggestions that appear in a national reference standard, the ANSI standard. That standard very explicitly says that instruments that differ from the calculated rate by more than 20 percent are out of calibration and should not be used.

It also talks about the use of calibration charts or reference tables for correction when the instrument is more than 10 percent out of calibration but within the 20 percent. That's why we say that the regulation that we have in place is generally consistent with the standard. In fact, it's a little looser than the standard because it doesn't require the calibration chart for those instruments that are between plus or minus 10 percent and plus or minus 20- percent from calibration value.

In practice, survey instrument calibrations, as most of you certainly already know, are usually done with a high energy source, regardless of the average energies of the photons in the fields that are being assessed. That need not be the case because the

calibrations simply suggested in the ANSI standard to be done with a source which is comparable in energy to that which is being measured. In practice also many energy dependent instruments and there are plenty of them available, that are calibrated with high energy sources, can respond within the plus or minus 20 percent limit when they are being used in a low energy field, and they often read conservatively high.

Now, there -- I'm not saying that every instrument will but there are certainly quite common instruments or probes which are available to be fitted to survey instruments which are also commonly available which will fulfill this limitation that appears in the regulation. I had general knowledge of these before. I contacted various manufacturers and got calibration curves and there are energy compensated Geiger counters for example. There are pancake probes with filters. There are scintillation type probes that are available which will when calibrated with a high energy source, enable the licensee to use them in low energy fields, i.e., iodine 125 is the most common one of concern.

I will also note that there are instruments undoubtedly that fulfill the requirement of plus or minus 20 percent, those that are based on ion chamber type measurements and the sensitivity of those is satisfactory

for the kinds of surveys that are required. For those people or those licensees that choose to use a more specialized probe for dealing with low energy sources for example, a low energy gamma probe, which would not fulfill the plus or minus 20 percent, if it was calibrated with a high energy source, the option for those in practice for medical use is to calibrate that instrument with a low energy source and this doesn't mean a great expenditure of funds or resources because calibrated -- because sources which are traceable to NIST are available at the institution in the form of Iodine 125 seeds, which could be utilized for the calibration of such specialized probes.

So the bottom line of it is that this requirement in the regulations is not onerous and should not require additional expenditures necessarily or significant additional expenditures on the part of licensees in order to conform with this.

CHAIRMAN CERQUEIRA: Jeff?

DR. WILLIAMSON: Yeah, I'm just a little hazy what problem is that your presentation is addressing. Is it that if one has a low energy probe and to make it accurate for low energy gamma fields, you have to calibrate it inaccurately on a cesium calibration range? Is that the issue that --

DR. ZELAC: The issue is primarily that there was a great deal of concern which was expressed by various professional organizations including the AAPM, that this was a requirement which was going to be unduly burdensome on licensees because they would, by necessity, in order to conform with this requirement, have to go out and purchase additional instruments, have multiplicity of instruments available to satisfactorily meet this requirement.

DR. WILLIAMSON: Well, it doesn't sound like you would. If I read -- that's why I asked my earlier question. It seems to me all you're stating is that whatever source you use to calibrate the ion chamber with, you know, the ion chamber better agree with it, within 20 percent. And you're not making the requirement that this calibration source match the radiation fields around the patient that are being matched.

DR. ZELAC: That's exactly correct and that was part of the argument that was put forth by professional societies, that the instruments that they do have available are all calibrated with high energy sources and therefore, could not meet this requirement and they, therefore, would have to go out and purchase additional instrumentation.

DR. WILLIAMSON: I'm still confused what the

problem is.

DR. ZELAC: That's the point, I don't think there is a problem.

MR. LIETO: A lot of instrumentation that's out there, though, does not meet the plus or minus 20 percent. For example, if you're doing -- you've got an HDR unit and you've got a survey meter calibrated at the high energy as Ron pointed out, you're fine. But if you take that same instrument and you start doing surveys for patient release or whatever for I-125, you're going to have a difference that's much, much greater than 20 percent.

DR. WILLIAMSON: But the law doesn't address that.

MR. LIETO: Well, I think that's what the question that they want guidance on and response to that if you have an instrument that's calibrated at cesium and it's well within the plus or minus 20 percent, if you use it at different energies from what it is calibrated at, making corrections for the chamber based on say the manufacturer's, you know, energy response curve, does that still comply with NRC and meet the regulation, that's the question mark.

DR. ZELAC: And the answer to that is no, it does not.

DR. WILLIAMSON: Yes, it does.

DR. ZELAC: No, it does not because you cannot use the information from the manufacturer as to the energy response. What the regulation says is that the response of the instrument is within 20 -- plus or minus 20 percent.

DR. WILLIAMSON: In the calibration field, so you're telling us that if we calibrate an instrument with cesium 137, it's zero percent off, we can go and use it for an I-125 patient and measure the exposure rate and write it down, but we're committing a violation if we make a correction for the energy response at that energy. That's a violation?

DR. ZELAC: That's correct.

DR. WILLIAMSON: That's insane.

DR. ZELAC: Now you know what the issue was.

(Laughter)

DR. WILLIAMSON: So where does it say that it's illegal to apply an energy response --

MR. LIETO: And I think that's one of the points that Ron -- that this was brought up is that in the previous version of Part 35, you were allowed to apply --

DR. ZELAC: Absolutely, you were.

MR. LIETO: -- corrections.

DR. ZELAC: And now you are no longer.

MR. LIETO: And in Part 35, somehow that specific -- that specific sub-rule was eliminated.

DR. WILLIAMSON: Where does it say you can't apply corrections in --

DR. ZELAC: It says the response of the instrument. I could turn -- I'll paraphrase it. The response of the instrument has to be within plus or minus 20 percent.

DR. WILLIAMSON: Of the calibration field.

DR. ZELAC: Right.

DR. WILLIAMSON: But not the field around the patient. I'm reading the -- you know --

DR. ZELAC: "A licensee may not use the survey instruments if the difference between the indicated exposure rate and the calculated exposure rate is more than 20 percent".

DR. WILLIAMSON: That's why I asked you, what does "calculated exposure rate" mean? And you said it meant the calculated exposure rate in the calibration range. So that's a cesium 137 source. That's not an issue. All it's saying is and I think the intent of the regulation was this; that the instrument needs to be properly calibrated and it's up to the user to make adjustments or appropriate decisions, you know, what kind

of instrument and how to correct it for use in a different radiation field. That's only good practice. The only thing that's prohibited is to correct the original calibration. That's how it's always been.

DR. ZELAC: We'll have to take another look at it.

CHAIRMAN CERQUEIRA: Dr. Vetter and then we have a comment from the back and then Ralph.

DR. VETTER: Perhaps some people are taking this all too seriously. The purpose of this section of the regulations is to assure that if a licensee uses an instrument to demonstrate compliance, not to take accurate physics measurements, but to demonstrate compliance, that the instrument is calibrated to within plus or minus 20 percent of the calibration source. And then you can use it -- you can -- I mean for purposes of physics, if you want to apply a correction package, you can do that, but you don't need to for purposes of compliance, and this is addressing a compliance.

DR. WILLIAMSON: Let me say further, that you can't apply corrections for differences in quality for --

DR. VETTER: Not for purposes of compliance.

DR. ZELAC: One could make the argument and I think that's why we're having this discussion that

Section B, which is what we're talking about, when it says "calculated exposure rate", it's talking about the exposure rate that you might calculate in that particular field of use.

DR. WILLIAMSON: That's why I asked you what --

DR. ZELAC: I know and I gave you the answer that I thought was appropriate but on second thought I'm not sure that that was the intention.

CHAIRMAN CERQUEIRA: In the back microphone if you could state your name and who you're affiliated with.

MR. WHITE: Thanks, my name is Jerry White and I'm going to speak for the AAPM, American Association of Physicists in Medicine. And I guess I'm going to disagree with almost everybody. I think -- first of all maybe I'll agree. I believe that the NRC's position is that the reading on the survey meter must be within plus or minus 20 percent of the true reading in the radiation field that you are measuring, irrespective of the calibration source energy that you used. So I think that's clear.

And then I'll disagree with Ron that this is not a problem. It is a significant problem for hospitals who use a wide variety of energy sources. A nuclear

medicine department surveys iodine 125 through molybdenum 99. The ionization chambers that have a flat energy response are not adequate in sensitivity to measure through that range, so you would need Geiger probes with -- you would need an array of Geiger probes for all the compliance issues that you have to measure and the same in radiation therapy. It's a significant problem, I think.

DR ZELAC: Well, I clearly disagree because I said before on this one I'll hold up to. I think that the sensitivity of an ionization chamber instrument is adequate to meet the requirements and to serve effectively for the kind of survey measurements that you need to make. And on that basis one could have a single instrument. You don't need necessarily a multiplicity of instruments. However, for those facilities that already have a variety of instruments. I think: (1) it depends on what it is as to whether or not it would meet the plus or minus percent in the field being measured, and; (2) if it doesn't, there are not expensive modifications such as buying a different GM probe that will.

DR. SIEGEL: I don't want to spend a lot of arguing, but in the field it doesn't work that way. You purchase a new GM probe, you still have the GM rate meter. And it's the rate meter that --

DR ZELAC: You have to make that the calibration is right at anytime.

DR. SIEGEL: But when the technologist measures their technetium in the morning and then measures them the molybdenum in the afternoon. They can recalibrate the rate meter.

DR ZELAC: No, they're not supposed to be recalibrating it. That's the point. If you have a probe which is essentially acceptable in terms of response over a broad range of energies; IM chamber, an energy compensated GM chamber, even pancake GM chambers with filters on them you don't have to do any recalibration. You calibrate it once with the high energy source and use it where you need to use it.

CHAIRMAN CERQUEIRA: All right. So Ron says it's not a problem. Ralph?

MR. LIETO: Dick, correct me if I'm wrong, but when you calibrate these, okay, there's only one pot setting per range on the instrument. So if you put in a probe and you calibrate it for I-125, okay, and you adjust the pot settings for 125, you put a new probe in those pot settings, they have to be redone. You have to send it out and have it recalibrated.

DR ZELAC: I agree. What I was saying is that, first, there are instruments available which will

satisfy this requirement.

Secondly, there are also probes available that can be purchased for existing instruments that will satisfy the requirements.

The last resort, as I was saying, is to take a probe which intended specifically for the low energy and calibrate it for the low energy and only use it with the low energy.

CHAIRMAN CERQUEIRA: Ralph?

MR. LIETO: But I think the issue, Ron, is the fact that before Part 35 revision everybody was out there and in compliance. Part 35 revision, this gets dropped, okay. And whether it should have been caught or whatever, okay, or whether it was intentional or it wasn't realized the ramifications of this.

DR ZELAC: Let's put it this way. There is an ANSI standard out there and we're obligated to have requirements that conform with the ANSI unless there is a valid bona fide reason for not. And I'm not sure from our perspective there is a valid bona fide reason.

MR. LIETO: The ANSI standard is in the methodology of calibration, if I'm not mistaken. Not the fact that you can't have a calibrated chamber and apply correction factors to that. I believe that -- I don't want to misspeak for the therapy fellows, but I am almost

certain that they very often will get a calibrated chamber and then they make correction factors for various things that are applied to it to meet the accuracy that they need. So --

DR ZELAC: The ANSI standard permits that as long as the response is within plus or minus 20 percent. If you're within plus or minus 10 percent, you don't need any correction factors. If you're between plus or minus 10 percent and plus and minus 2- percent, you should apply a correction factor. If you're beyond plus or minus 20 percent, they say the instrument is not calibrated.

MR. LIETO: Well, that's what we're trying to reflect in this standard.

CHAIRMAN CERQUEIRA: Dick. This is a very technical issue here and some of us could --

DR. VETTER: This entire section, 35.65 deals with calibration of survey instruments. It does not deal with fields in the work environment or around a patient, or whatever. It talks about how the instrument shall be calibrated, it talks about the scales and so forth.

Paragraph B certainly was intended to refer to the indicated and calculated exposure rates from the calibration source, not out in the work environment. I

mean, there are many cases where you wouldn't be able to calculate a field -- or if you could calculate something, but you'd be way off in terms of what you would expect out around a patient or in the work environment. So this clearly deals with calibration.

DR ZELAC: I agree with your comment, this does deal with calibration.

CHAIRMAN CERQUEIRA: So do we have a problem or don't have a problem, I guess?

DR. WILLIAMSON: Well, we do because he says it's illegal for us to make any kind of a correction for differences between calibration and patient environment. And I think that that's --

CHAIRMAN CERQUEIRA: If that's a problem--

DR. WILLIAMSON: You're basically stating that you're requiring us to follow a bad practice. And I think in many cases the most prudent thing to do would be to allow a user to exercise his or her professional judgment and make a correction, not to the basic calibration, but for differences in quality. We do that in calibration of therapy. Proton beam and electron beam sources all the time. The calibration particles specify. And here we're talking about a radiation safety issue where the level of precision required is not 2 or 3 percent, but probably 10 or 20 percent as an acceptable

precision. So, you know, it seems to me you should, you know, think about what best serves the clinical practices --

CHAIRMAN CERQUEIRA: So is that some things you can do, Ron, I mean --

DR ZELAC: I'll repeat what I said before, we'll revisit the issue.

CHAIRMAN CERQUEIRA: Okay. All right. We have a couple of comments from the audience.

MR. FORREST: Hi. Robert Forrest, University of Pennsylvania. I would wholeheartedly agree with that because I think in practice many dentists and places only have, for example, a GM meter and for whatever. And for past experience, that's what they've used. And now if you're telling them that they have to calibrate it for each different source, that would be a change in practice because most of them are calibrated to a caesium source.

In addition to that, saying that they need or they could make this measurements with an ion chamber differs from 35.70 which says you need to make the measurements with a radiation detection survey instrument. And previously in Reg Guide 10.8 Rev. 2 radiation detection instrument was defined as a GM type meter and a ion chamber.

DR ZELAC: 10.8 is superseded by 151156 Volume 9.

MR. FORREST: Okay. But I would imagine still that a radiation detection survey instrument was defined as a GM and not an ion chamber. So either you have to come out with a statement that says you're no longer in compliance, you used to have a GM meter, now you need an ion chamber. And in addition to that, you need to calibrate for ever energy you may be using, which as several people have pointed out and we've had this discussion previously of yttrium measurements. When you're talking about Bremsstalung, you're talking about every conceivable energy, so what would be the proper energy there. I think it's a bigger can of worms than just making a statement with that.

DR. WILLIAMSON: And it would force people to use an ion chamber survey meter when they're trying to detect minuscule amounts of radioactivity and contamination. So I think if you held to the most extreme interpretation that has been mentioned, not necessarily by you but by others, for example indicating that paragraph B refers to the agreement in the patient radiation field could actually harm safety by forcing -- encouraging people to use instruments that aren't sensitive enough for the purpose.

CHAIRMAN CERQUEIRA: So how do we resolve this, Ron.

DR ZELAC: I think it's pretty clear from the feedback based on this presentation that we have to revisit the issue and then you have --

CHAIRMAN CERQUEIRA: Revisit in what way?

DR. WILLIAMSON: And you give us some assurance, yes.

DR. ZELAC: I mean revisit it in terms of discussion and consideration of it. We can report back to you as to what the outcome is of our consideration.

CHAIRMAN CERQUEIRA: Dr. Nag has suggested a subcommittee to look at this.

DR. NAG: Have a physics subcommittee and involve the members of the --

DR. ZELAC: You're the advisory committee, do as you wish.

DR. NAG: I mean, I didn't understand anything of what went on. And I don't know much the others did.

CHAIRMAN CERQUEIRA: No, but obviously it's an important issue for the regulated community. I hate to form more subcommittees if we can just get a resolution. But it doesn't sound -- I mean, what sort of input do you need? I mean, you've heard all the

comments.

DR. ZELAC: I don't think you need anymore input. I think we have sufficient amount of input and we'll just have discussions at staff level about what this all means.

CHAIRMAN CERQUEIRA: Okay. So maybe you could come back at the next meeting and report on it?

DR. ZELAC: Yes, sure. Right.

CHAIRMAN CERQUEIRA: And do you want input from the committee?

DR. ZELAC: I think we have it in the transcript.

CHAIRMAN CERQUEIRA: Yes. Well, maybe we could have Ralph, he doesn't have enough to do currently and is looking for more things. So maybe you could interact with him to provide some musical information. And that way we could just -- okay. Great. Excellent. Thank you.

DR. ZELAC: Okay.

CHAIRMAN CERQUEIRA: All right. The next item is a "Review of Medical Area Operating Experience and Enforcement Actions. One year and Since 10/24/02"

What does all that mean?

MR. ESSIG: We are discussing Mr. Torres' sore throat. He almost didn't make it today. So,

hopefully he's going to be okay.

MR. TORRES: I'm okay. Thank you.

Well, good morning, members of the Committee. The title: Medical Area Operating Experience and Enforcement Actions. What does that mean? Well, in plain language has the Part 35 rule significantly changed the number of enforcement actions on reported medical events? That's the question. And the short answer is that it is too early tell, but let's see the data that we have right now.

The numbers that you are going to see shortly, they come from the Nuclear Materials Events Database.

CHAIRMAN CERQUEIRA: We have the slides in front of us, so why don't you go on --

MR. TORRES: Okay. The first slide has the data for misadministrations for 2001 and '02. And as you can see 10 events, 16 and 17 respectively.

After the implementation of R-35 on October 24 the last part of the year 2002 we had one event and for the year '03 8 so far, up to April 18, '03.

The second slide I'm going to use -- I'm going to focus on enforcement actions in which escalated enforcement action was required. And before going over the slide, let me briefly explain what does that mean.

NRC has different type of severity level violations. Severity level violation I through IV. One the most severe, IV the less severe.

Escalated enforcement actions are considered dose severity levels I through III.

So for --

DR. WILLIAMSON: I'm sorry. What was I through III?

MR. TORRES: One through III is considered escalated enforcement action. The severity increases which is severity level.

So for the year 2000 we have from those ten events --

CHAIRMAN CERQUEIRA: Can you advance your slides then if you're going to show them?

So the slide for year 2000, what type are those?

MR. TORRES: This is the year 2000. And from the ten events that happened, medical misadministration, two involved diagnostic nuclear medicine, one therapeutic nuclear medicine and two events involving remote afterloaders.

I want to point out that the severity level III violation occurred from the failure of the technology to verify the recent directive. And severity level III

violation involve when there is a programmatic failure unidentified in the program. But let me step back. Not every medical misadministration or medical event will automatically trigger a severity level violation. If during inspection it is determined that a medical event or medical misadministration is a result of violation of an NRC requirement, primarily Part 35, then most of the time the licensee will be cited against a severity level IV violation.

As I mentioned before, it is determined that there's a programmatic failure, several instance in which there were medical events, then it will be escalated into III.

DR. WILLIAMSON: What about II and I

MR. TORRES: The next slide shows that only one gamma knife event involving in which there was a medical misadministration, that one in which the coordinates were transposed, that was a severity level IV violation. It's not on the slide, but you can make a note of it.

On the manual brachytherapy for the year 2000 4 events occurred, two of them ended by as being cited as a severity level III violation. Both of them because there was a failure to written procedure in the QMP.

For the year 2001 and there were no medical misadministration under diagnostic nuclear medicine. Four on the therapeutic nuclear medicine. The first two bullets under therapeutic, failure to verify a written directive in two of the events and a technologist failed to administer a full dosage. Both of them as ended up as being cited a severity level IV violation.

The third one which involved 65 patients which received under dosage of samarium 153 and there were 9 hospitals involved, this is a particular interesting case because the radiopharmacy failed to dispense correct doses. Nine hospitals received those doses and the hospital followed their own procedures and they administered those dosages to their patient. They followed their own procedures.

Who failed? The radiopharmacy. So it was the radiopharmacy who was cited here, not the hospitals.

DR. NAG: This is very systematic, it's not just an incidental. Could you give a little more background about how 61 or 65 systematic problem?

MR. TORRES: I don't have the details of the events, but I can get it to you right after this presentation and I can share it with the committee.

For gamma sterotatic radiosurgery, only two events happened.

Next slide, please.

We're still in the year 2002 and events -- medical misadministration involving HDR units, there were five events. Two of them were cited as severity level IV violations. They ended up as being -- ended up in our final enforcement actions.

Those two that received severity level IV violations were the incorrect entry of -- well index correct data entry into the treatment planning system. And the last one, which is an intravascular brachytherapy event, failure to follow the established licensee procedures.

CHAIRMAN CERQUEIRA: As somebody that doesn't do these, maybe my colleagues from radiation oncology, how many of these put patients at risk either from over exposure or under treatment? Those five events?

DR. NAG: I don't think I can comment unless I know the details. For example, with high doses like the first one, it depend on the dose whether you're giving 200 centgray, 500. Most commonly that would be because it came from -- so you're reading either double or event -- so with just this, I don't think anyone would like to say anything.

CHAIRMAN CERQUEIRA: Now would you put these

into levels? I mean, what level were these at?

MR. TORRES: The first one suffering -- the step size was inadvertently entered. There was no severity level violation associated with this event. And if the committee agrees, I can show you each description later on.

CHAIRMAN CERQUEIRA: Well, again, I'm just trying to get a feel for, you know, some of these are sort of administrative failures and some of these could really represent --

DR. WILLIAMSON: Well, I think most of them he's mentioned are really errors, but sometimes they happen through at least no regulatory fault of the individual. They were following all their procedures and it was, for example, an isolated error maybe by one individual. And if you thought, you know, the individual's training and so on complied with the regulation, there wouldn't be a citable offense

MR. TORRES: Right.

DR. WILLIAMSON: So, you know, I think -- this is an area where from a quality assurance perspective and regulatory perspective it's not identical. You know, surely we all in radiation oncology we have a much more vast QC system and infrastructure than anything NRC has ever imagined imposing on us.

CHAIRMAN CERQUEIRA: All right. Okay.

DR. WILLIAMSON: So, you know, you have to look at them from different perspective.

CHAIRMAN CERQUEIRA: Right.

MR. TORRES: I agree with you.

So following on to the next slide. On manual brachytherapy in the year 2001, again, we have five events and I don't have the data for the last one. Dose less than prescribed.

DR. WILLIAMSON: Are these medical misadministrations now?

MR. TORRES: These are still medical misadministration.

DR. WILLIAMSON: Okay. Okay.

MR. TORRES: Since we are in the year 2001.

DR. WILLIAMSON: But they are misadministrations?

MR. TORRES: The information I pulled from the Office of Enforcement, they have a database in which every code at whether they -- there was a final enforcement action or not. And there was no final enforcement action in any of these cases.

DR. NAG: I think that number 5 that that may be very relevant because we were talking about the permanent implantation so that the dose less than

prescribed of the seed implantation would be a matter of totally interpretation as to where you do the volume. That may or may not be, you know -- that's what we were discussing earlier in the morning, that sometime in the permanent implant it will depend very much interpretation of where the -- is and the dose that comes out after implantation --

MR. TORRES: In one of my last slides I will talk about two cases involving implantations. And I will expand on those.

We're in the year 2002. Before the implantation of the revised Part 35, and there were no gamma knife events, no therapeutic or diagnostic nuclear medicine events involving misadministrations.

We only had 4 HDR events. And as you can see, they all consisted of intravascular brachytherapy. Equipment failures, the use of a different catheter and the catheter did not reach intended site. None of these events ended up as being cited with any of the severity level violations.

The next slide there were three medical events involving manual brachytherapy. And the only one that was cited as a severity level III was the last one, the authorized user dropped the source. There was an inaccurate survey made. The source fell on the trouser of

the physician. The physician carry the source around the hospital. He get some exposure-- got some exposure, but it wasn't an overexposure. So that ended up as being cited as a severity level III.

DR. NAG: By the way, patient moving and patient dislodging not misadministration. It does not come under the admission of a misadministration.

MR. TORRES: This one patient move, involving patient intervention, well it was captured as being reported as a medical misadministration.

DR. NAG: It is not. If the patient --

CHAIRMAN CERQUEIRA: In the new rules it is.

MR. TORRES: Under the new rules.

CHAIRMAN CERQUEIRA: This is the old rules.

DR. WILLIAMSON: But even under the old rule, usually a patient intervention that was appropriately detected by the care provider and did not involve an avoidable technical error according to the guidance that we've had for many years is not a misadministration.

DR. NAG: Right. I mean, the patient will end up getting the lower dose, but that is not a misadministration.

DR. WILLIAMSON: No.

MR. TORRES: Ended up getting to the

intended target, but some other target --

DR. NAG: Right. Right.

DR. WILLIAMSON: But it's not a misadministration. I believe that there was published guidance at the time which excluded those events. And the only cases where I'm aware that were brought up and discussed in this committee over the years were those where fault was found with the caregiver in properly detecting that this had happened and, you know, basically responding to it inappropriately. And that was sometimes cited and then called a misadministration because an act of the patient that is not in control of the provider of care in is appropriately detected and corrected for, according to the standards of practice, should not be even under the old -- under the interpretation of the old misadministration rule being misadministration.

MR. TORRES: Right.

DR. VETTER: I beg to differ. I think the old regulations required that they be reported and region received guidance that they could make their interpretation. They could interpret then whether or not it was a misadministration.

So in this case, apparently, it was interpreted that it was a misadministration.

MR. TORRES: And indeed it was reported as

a misadministration and captured in NMED. And as of April 18 it was still there. And this is an event that happened in the year 2002. So updates -- the updates are there.

The next slide is the last two months of the year 2002. And this is now after the implementation of Part 35 and this data is from nonagreement states -- states under NRC has jurisdiction. So there was a reported event involving manual brachy in which 35 patients received doses, 32 patients greater than prescribed.

What happened here was the licensee sent the source to the United States for calibration. The source was returned to the licensee. The licensee choose a perimeter when calculating the dose to the patients.

Here, this event it's too early to determine if there's going to be any enforcement action. The inspection report is pending and a medical consultant was hired to assist the NRC in making this determination.

Now we're in the year 2003. 2003 there is one medical event report in the diagnostic nuclear medicine area in which a 9 year old patient received 400 microcuries of iodine 131 instead of a prescribed 4 microcuries. And, again, this event it's under medical evaluation and pending any enforcement action, if there

is any that is warranted.

In the therapeutic nuclear medicine area there was one reported event in which the technologist failed to administer the complete dosage. She didn't extract all the iodine 131 from the vial. He left some amount in the vial.

Up to April 18th there are no gamma knife events reported to the officer and there are 4 HTR events in which two of them involves intravascular brachytherapy and it's too early to determine what actions will be taken against this licensee, if any.

Well, we have two more cases for the year 2003 involving manual brachytherapy. And these are the two cases that they are under our Office of General Counsel review to determine if they're medical events or not. And both of them, they're very similar. It involves iodine-125 permanent implants to prostates. The implant were -- the seeds were implanted in a place other than the prostate.

DR. NAG: I think this is where you might want to seek the input and not just the general counsel, but the people who are doing the implant, which would mean the radiation oncologist because depending on how you -- intended area, you put the implant in just the bottom of the prostate and, you know, so there is room of

interpretation and we need more details than just this to make an idea.

Now, if you're intending to implant the prostate and you implanted the head or neck, I mean that's a different thing. But if you intended to implant the prostate and you implanted the base of the prostate and not the apex, that's the different thing. Then we need more details.

MR. TORRES: I can provide more information right now.

The first event in which involved 4 iodine-6, the first bullet, the intended area was the bladder. And the second one in which 100 percent dose was given to an intended site, it was the bulb of the urethra.

DR. NAG: But, I mean, that is the nature of the way you do implant. I mean, you are going to have some seeds in the bulb of the urethra, which is just below the prostate. And when you go higher you are going to have some seeds in the bladder which when you -- you may not.

DR. VETTER: Not 42.

DR. NAG: No. Okay.

DR. NAG: The amount is quite a bit.

CHAIRMAN CERQUEIRA: But by this time Dr. Miller's probably wondering what all the hoopla is about.

I mean, he's used to nuclear reactors and this seems relative trivial. Either we have a program to work --

DR. MILLER: It wouldn't be if it was in me.

CHAIRMAN CERQUEIRA: Although, you know, the thing is some of these things in terms of -- you know, if you overdose or underdose you run into problems. Some of these things are sort of administrative. And, obviously, you know you need to monitor the programs to make certain that these things don't generalize into more severe events. But in terms of outcomes to the patient, is it adverse because it's lack of treatment or too much treatment, this is relative minor.

DR. MILLER: You know, Roberto, it might be worth just reminding everyone for just a second how we get this information with regard to events. In other words, I think there was some discussion with regard to, you know, whether it was a problem, whether it wasn't a problem, whether it violated its intended purpose, whether it didn't. But this information is reported to us by the licensee, correct?

MR. TORRES: All right. The information is reported --

DR. MILLER: He self reports himself for having done something wrong.

MR. TORRES: Right.

DR. MILLER: So it isn't something that we go in and pass judgment on someone. That's our starting point --

DR. NAG: Right. But then the next point is, you know, when you're going to make an examination what level, you know, what is the problem, what level and that's the place where I think you should be involving us.

MR. TORRES: Right.

DR. NAG: And, you know, rather than you making a determination and then we finding at later point that you came -- the problem and we are thinking it's not a problem or vice versa involvement from the beginning.

DR. WILLIAMSON: Well, to restate it a little different way, I mean I think you need at least a good medical consultant to determine whether this is within the normal limits of medical practice, how many seeds are in these regions versus not. You shouldn't I think be making this determination by yourselves.

MR. TORRES: Thank you very much for pointing that out. And I believe there is a medical consultant, but I will check that out and we will inform you.

DR. WILLIAMSON: It need not be us.

MR. TORRES: Right.

DR. WILLIAMSON: I mean, you have a system of medical consultants. And, you know, I think this we knew from the outset when we designed this regulation that for permanent seed implants, especially it would be really difficult to, you know, make an exact determination. So, you know, I think there certainly are cases where there might be a gross misinterpretation of the ultrasound image, and seeds to get put really in the wrong and it's a terrible bad implant from any radiation oncologist. And there might be other cases where, you know, it's not so clear that, you know, it's an issue of maybe of -- you know, could have been a difficult case and this was the very best that could be done or within the normal limits. I think that's what we're trying to say that it's a difficult determination. And no sharp regulatory criterion that you can be given.

MR. TORRES: From the information that we received from the licensee, which is in NMED, the license reported we misread the ultrasound in both of them.

DR. WILLIAMSON: Yes. Okay.

DR. BRINKER: My question was only do you get a narrative with the report? In other words, do you get -- and I think you've just answered it. You get a written explanation and clarification at least from the site rather than just we misadministered?

MR. TORRES: We have a detailed explanation of each of these vents in our NMED database.

DR. NAG: Is it possible or at least for me, is it possible for us to get a copy? This is something we do everyday and we would like to know why this happened and how it happened.

DR. WILLIAMSON: That would be interesting background material for us.

MS. WILLIAMSON: Angela Williamson.

I would also like to point out to the committee when these events happen, an inspector goes out and there's a follow up inspection what occurred. Gets a lot of information on the specifics of what occurs and that on site visit plus the interviews with the licensee also factors into whether or not the event meets our definition of a medical event. So it's not just a matter of us having some paperwork in front of us and the paperwork is a narrative. But it's not just a matter of us having a narrative in front of us and making a determination based solely upon that narrative. We do conduct follow-up actions that verify and help us determine whether or not this is truly a medical event.

DR. NAG: Is that a medical person who does that. And if not, then I think it would be nice if these people went through either a consultant or one of us.

CHAIRMAN CERQUEIRA: I think what all we're saying is if you've got medical expertise on this committee that has a little bit, you know, greater understanding of the eventual consequences to the patients or the public. And to not use that information really minimizes, you know, they're valuable to the site as well as to your monitoring for these events. And it would be useful to use the committee or the outside consultants.

MR. TORRES: Your point is very well taken.

DR. BRINKER: Can I ask one other question? Have you ever estimated, and I hope you acknowledge this to be true - maybe you don't - how many misadministrations or medical relevant problems occur that are not reported to you? Has anybody ever tried to get a handle on non-reporting things even if it should be reported?

DR. MILLER: Well, we would only know of a nonreported event if it's somehow uncovered by some other means.

DR. BRINKER: You know, like --

DR. MILLER: Well, when you do a visit to sites, I mean, you know we're not doing very many of those. You would sometimes pick those things up from logs that weren't reported.

MR. TORRES: Right. Right.

DR. MILLER: Sally, you had a --

MS. SCHWARZ: I just have a question of clarification on your misadministration for 2001 on the 61 patients for the samarium. What actually caused that to occur?

MR. TORRES: The radiopharmacy somehow use -- didn't calculate -- didn't account the beta radiation and the plastic, the shielding of the plastic syringe, didn't use a correct factor in their calculations.

CHAIRMAN CERQUEIRA: Okay. Other questions for Mr. Torres? Yes? Oh, we have a comment from Dr. Siegel.

DR. SIEGEL: That was a very interesting presentation. Just one question. I'd like for you to comment on -- my name is Jeff Siegel, by the way, from SNN/ANCP.

Given that diagnostic nuclear medicine sees 14 million patients and does 16 million procedures a year and that your reported medical events or misadministrations was two zero zero and one, what comment do you have about that? I mean, is that good, is that what you would expect. Is that bad?

MR. TORRES: I don't have the corporate knowledge. I only been with the NRC for 4 years, so your

question will be better answered by somebody who has previous operational experience before that year 2000.

MS. WILLIAMSON: This is Angela Williamson.

We have certain metrics that we have to meet for various types of events. And we do have a standard of -- we do have a limit of the number of medical events that should -- that we determine should occur per year.

So I guess the answer to your question, at least from our regulatory perspective is that the number of number of events that occurred are below our metrics. And that's good. Obviously, we would prefer that none of these types of events occurred, but for regulatory purposes the regulated community is performing well.

CHAIRMAN CERQUEIRA: Yes. I guess what's implied in Dr. Siegel's question is either you guys are doing a great job in keeping the events low or you're spending a lot of money monitoring something that is so safe that it doesn't need to be monitored.

MR. TORRES: I would like to add that this presentation is basically focused on Part 35 violations. When I review the data from the Office of Enforcement there were other severity level violations cited against hospitals, but they were Part 20 requirements.

CHAIRMAN CERQUEIRA: Yes. So I guess we're

just seeing self reports, but the enforcement actions which again it gets back to the question I think Jeff asked, how many of the events occurs that aren't reported; that would start to deal with that.

MS. WILLIAMSON: And I would also like to point out that what we are keeping track are requirements from Congress. I mean, we don't have the option to not keep track of it at this point. We have to report the -- monitor these numbers and report them.

CHAIRMAN CERQUEIRA: Jeff?

DR. WILLIAMSON: Well, yes. And even when I read your report coming here and as I've been listening, I'm reminded of past ACMUI motions and recommendations. And, you know, I guess what I would recommend, and I think this committee should consider recommending to NRC as a formal motion, that when you present this data, you should give us indication of the denominator. Because you're looking at changes from two to five, eight to ten and you're going to be actually making possibly some judgment about the direction of regulatory initiatives based on very small numbers. I think it behooves you to understand what the denominator is. Because if a field expands rapidly, as prostate brachytherapy has, it has gone from 5,000 procedures a year in 1995 to somewhere of the order of 40,000 to 50,000 patients. It's become now

almost a dominant treatment for low risk prostate cancer.

And so when you look at the number of misadministrations or medical events for this disease category, I think you need to look at the risk ratio. So somehow you need to take the number of events that you're tracking relative to the estimated number of treatments or procedures given. That's the only meaningful way, I think, to look at year-to-year trends.

CHAIRMAN CERQUEIRA: Right. And then to factor in the medical consequences of these problems I think is also an important factor.

One last comment and then we should break for lunch. Yes.

DR. HEVEZI: One comment.

CHAIRMAN CERQUEIRA: Sure.

DR. HEVEZI: I'm Jim Hevezi representing ASTRO. And I'd like to make a comment.

Again, I agree that denominator should be used here. In agreement states we make these reports and in the investigation one of the things that the institution has to do is to tell the agency how we will try to minimize this occurrence in the future. And I think that's a useful thing to have to do in these areas.

CHAIRMAN CERQUEIRA: Donna-Beth?

DR. HOWE: I just wanted to make a

historical comment, and that is that back in 1992 when we did the quality management rule, at that point we were getting at least 400 diagnostic misadministrations a year. The medical community made the argument that even though we were getting 400 a year, they were not significant events. And so we redefined the diagnosed misadministration to put the threshold higher. And the concept was that the threshold would be where we wouldn't get any -- difficult to get a diagnostic misadministration.

We have gotten a few with technetium generators where they deliver the entire eluent to a person, and we have gotten ones primarily in the microcurie of I-131, which would have been in the diagnostic.

So, to answer his question about the diagnostic nuclear medicine, the threshold is essentially so that these are really egregious cases to be popping up. And the brachytherapy has stayed pretty much the same, but we're seeing those more now because they're not being hidden in the 400. They're standing out.

DR. WILLIAMSON: Well, I'd like to ask if, you know, we want to take seriously my suggestion as a motion, Mr. Chairman.

CHAIRMAN CERQUEIRA: Can you restate the

motion?

DR. WILLIAMSON: The suggestion is that in receiving -- in giving reports of this nature the NRC make some effort to estimate the denominator and present a relative risk or hazard rate or basically fractional incidents as well as absolute number of adverse events, medical events or severity violations so that the data can be understood in perspective.

CHAIRMAN CERQUEIRA: Roberto, do you have that information? I mean, have the number of diagnostic procedures or therapeutic --

DR. MILLER: I'm not sure if we have that information.

DR. WILLIAMSON: How can you get that?

DR. MILLER: We don't collect that information as a matter of regulation.

DR. WILLIAMSON: But it can be estimated. Okay. And you've done it before because it was done at the request of the ACMUI once before when assessing the adequacy of the --

DR. MILLER: Well, you have historical data. There's a whole bunch of groups out there that monitor primarily for industry the frequency of testing and other things.

DR. WILLIAMSON: So you've done it before.

DR. MILLER: Okay. Let me respond to what you said. If we don't have the data at hand, then that means that we have to expand resources to collect the data. And before I'm going to expand resources to collect the data, I need to know what the value of it is to the committee with regard to, you know, being able to advise us.

I mean, I think in one sense I think you all have a sense from working in the industry how many of these are done very year. If you see the data reported up here, and there's a very few of them, I think that gives us all a sense that the procedures are being done very safely overall. You know what I'm saying?

DR. WILLIAMSON: Yes.

DR. MILLER: If that data gives us information that we can use collectively to help us frame the regulatory structure in the future, that's great.

DR. WILLIAMSON: Well, I think it does. I think what it will show you if you normalize the -- took just permanent seed implants, you know, my guess is that you would find the rate is precipitously maybe has fallen, perhaps, a factor of 5 or an order of magnitude. Maybe the absolute number of misadministrations or enforcement actions is, you know, roughly the same or increasing slightly, but you know given that the number

of patients treated has increased annually by a factor of ten, that's important information for you to know in interpreting this data.

CHAIRMAN CERQUEIRA: Yes, it's hard data to get. You know, I think the professional medical societies usually have some of that information available. I think they would be willing to provide it to you so you could get a feel for it.

DR. MILLER: Is there an avenue that you as doctors can aim us in?

CHAIRMAN CERQUEIRA: Well, again, all of us are usually affiliate.

DR. DIAMOND: We don't want to put you on a wild goose chase. If you want to do those numbers, it would take you 30 seconds to answer that and see -- or Prabhakar, we get that information to you in a general fashion, which is all you need.

CHAIRMAN CERQUEIRA: Yes. Yes. No, that could be done. For the cardiology procedures I'm sure that could be done. For the diagnostic --

DR. MILLER: I guess what I'm searching for not doing is going out and spending $50,000 or $100,000 which these studies sometimes cost in order to be able to get the data.

DR. DIAMOND: We just want to know if

there's 20,000 prostate plates a year or 100,000, that's all.

DR. MILLER: That's great.

CHAIRMAN CERQUEIRA: Yes, that could be gotten. And, you know, I think if you talk to us individually we can get you those numbers.

DR. MILLER: Great. Well, we'll do that.

CHAIRMAN CERQUEIRA: We should wrap up.

MS. SCHWARZ: What about Jeff's motion?

DR. WILLIAMSON: It wasn't a motion.

CHAIRMAN CERQUEIRA: It wasn't a motion.

DR. WILLIAMSON: Well, so moved.

DR. BRINKER: It was an emotion.

CHAIRMAN CERQUEIRA: All right. I think they've taken the point.

MR. MARKLEY: These are all very, very good points and I think we certainly need to take them back and put them in the right consideration. The numbers, and putting it in maybe a risk informed as opposed to a risk based context may be the right thing to do.

Clearly, looking at how the information and the context of risk fits is something I should be looking at within the context of the pilot and what should we be doing for diagnostics.

So, personally I thank you very much for

that and I will take that back and look at it.

CHAIRMAN CERQUEIRA: The risk is very important. And I think certainly this side of nuclear medicine has made the point that diagnostic is so safe that you guys shouldn't be involved, and Carol Marcus has made that point quite a few times. But I'm taking the opportunity to bring that up again.

So, why don't we try to finish up.

Ralph, you want to --

MR. LIETO: I was just going to ask Roberto, the information that you get from the agreement states, do you have -- I mean are the events that they find, are they all reported to you or do they -- or is there sort of any communication issues or informational issues that there may be investigative events that don't get reported to the NRC?

MR. TORRES: Well, agreement states report all the events that are required to be reported. But this is outside the medical area. They have to conduct some investigation. And at the end of their investigation, then they will submit the complete data. But the answer is yes.

And this is a slide that you have in front of it. It's the events that happen in the agreement states, medical misadministrations. And please note that

for the year -- the end of the year 2002 and 2003 the agreement states will be reporting to the NRC either medical events or misadministration depending on whether the agreement state has adopted Part 35 or not.

And the last slide shows you that Iowa has passed already, adopted revised Part 35. Wisconsin, which will become an agreement state this summer, they have the final rule in place.

And Minnesota and Maine, they have a proposed rule to adopt revised Part 35.

And with this slide, I finished my presentation.

CHAIRMAN CERQUEIRA: Good. I'd sort of like to make one comment. If you look at those events for the agreement states,which is what 32, probably the largest populations. So it's actually a very good record for the agreement states.

Dick?

DR. VETTER: I just wanted to thank Roberto for this report. It's very helpful. It's a measure of the effectiveness of regulations. And we're here to try to help you implement safe regulations. And you know, where are we in that effort? This really helps us to assess that.

DR. MILLER: Dr. Cerqueira, you made a

comment earlier concerning, you know, the various views. And Dr. Vetter, that's I think a good synopsis. I think when we look at these things we can conclude a number of things.

One, you know, one could conclude the regulations that we have in place are working to do the job. But more than that, we have to constantly in looking at the risk of these kinds of procedures, is there a regulatory burden that's being put on the licensees that if that regulatory burden were lessened, would still result in getting data like this or not. And that's not always easy to determine, you know. But I think it does determine that the regulations we have in place are adequate and at least don't need to be tightened down at this point in time for any reason.

CHAIRMAN CERQUEIRA: And certainly if you go back over the history of this committee and the Part 35 revision, I mean we felt that a lot of these things really needed to be lessened to a large degree. I mean, some of the practices have become so standardized and they're relatively safe that it has worked.

One last comment from Dr. Williamson, and then we'll go to lunch.

DR. WILLIAMSON: I just wanted to comment why I raised the issue is that I think it probably was

1995 or 1996 presented to this ACMUI committee was a report claiming that the quality management program was effective and what they were comparing -- they had actually put the denominators in and they comparing the misadministration rates before and after the imposition of the quality management program, which I guess was in the early 1990s. And, you know, it was like ten to the -- five times ten to the fifth versus seven times ten to the minus fifth. And the individual ludicrously concluded that the program was working effectively when there was no statistically significant difference between the rates in the two errors.

That experience, I think, effected my perception of this kind of data profoundly.

CHAIRMAN CERQUEIRA: Right.

DR. WILLIAMSON: And so I think to look at it critically from a statistical point of view and think about, at least at best you can, the size of the population and how it grows or contracts with time is really important.

DR. MILLER: As long as we put the right caveats on any information when we get to the total numbers. Because it's going to be estimates. Sometimes data has a tendency to be abused if it's taken and then republished and republished. The exactness of it has to

be made know. I think we all understand that.

CHAIRMAN CERQUEIRA: Dr. Eggli and some of the other people could give you specific information for therapeutic for diagnostic nuclear medicine. And you people should contact him.

We're looking at the schedule. And it seems like instead of having an hour for lunch, we got an hour and 50 minutes. I'd propose that we come back at 1:00 and then try to get this subcommittee some more time.

If any of the people in the audience have items and they're set for the time, just be aware that we are moving things forward.

Thank you. We'll break.

(Whereupon, at 12:15 the Advisory Committee was adjourned to reconvene at 1:08 p.m.)

CHAIRMAN CERQUEIRA: There are some items of housekeeping. There is a note left for most of you from I think Roberto Torres on informational tools, medical events involving I-125 prostate seed implants. So he's given us some very specific information on that.

In speaking with Angela, she needs those updated slides by today. I told her it's not possible. And I told her tomorrow would be the earliest we could get them to her.

DR. WILLIAMSON: I will have some draft

slides for you on the parts I'm obligated to give you today. But you'll have to put them in --

CHAIRMAN CERQUEIRA: No, no, you can e-mail them to me. That would be great.

DR. WILLIAMSON: I'm going to have to give you handwritten ones.

CHAIRMAN CERQUEIRA: Handwritten, okay. That's fine. Okay. And Mr. Thomas Essig had other pressing commitments that he needs to attend to for the rest of this session. And he apologizes, but took --

DR. MILLER: Well, he'll be back in a little while.

CHAIRMAN CERQUEIRA: Okay. All right. Then the first item is updates, recommendations from the Fall 2003 meetings. And Angela, I wonder if we should -- there's a whole bunch of administration conclusion things at the end, including next meeting date. I guess we need Angela for that. That would be usually in October.

We usually have it sort of the last week of October or so. I can't ...

DR. DIAMOND: So we're looking at the 28th of October?

CHAIRMAN CERQUEIRA: Yes, it's right around that time. How does that sound to most people. That's again a Monday-Tuesday, or Tuesday-Wednesday I guess.

DR. VETTER: It's a Monday-Tuesday. Twenty-seven - 28 is Monday-Tuesday. What about the previous week?

DR. DIAMOND: The previous week is ASTRO.

CHAIRMAN CERQUEIRA: Okay. These are all administrative things, but we'll -- So ASTRO is that week. That probably would be difficult. So -- This meeting we're having like Tuesday-Wednesday. Was there a reason for that? Do people like to travel on Sunday for Monday-Tuesday? That's preferable?

So the 27th-28th?

DR. WILLIAMSON: Of what?

CHAIRMAN CERQUEIRA: Of October. All right. So I'll have Angela send a note out to people just to make certain, and we'll try to confirm it. The previous week would be difficult because, I guess, of ASTRO, and then the week before that those people would probably be involved in preparation and activity as well.

So we'll try for that week. Hopefully the 27th-28th. I guess the other potential problem would be scheduling of the room.

DR. NAG: Is something else going on on that day?

CHAIRMAN CERQUEIRA: Well, that's the one thing that will have to be checked. We don't know, but

that --

MR. MARKLEY: We'll get the schedules for the ACRS, ACNW right away.

CHAIRMAN CERQUEIRA: Yes. If you could do it for October 27-28, that would ... And agenda topics I think are a little bit premature. And meeting summary. A good time was had by all, is that?

DR. WILLIAMSON: Were we going to try to have a telephone conference in between?

CHAIRMAN CERQUEIRA: Yes. Yes, so we do need to set a date. And I guess we decided it took about two months to get the transcripts, the minutes, and then some follow-up on the minutes.

DR. NAG: Early to mid-August?

CHAIRMAN CERQUEIRA: Okay. I mean, August is always a difficult month, but I think we can schedule a conference call for then. All right, I'll talk to Angela specifically about that.

And I guess Michael do you have any updates on committee member appointments? You know, sort of the process for the new people, or I don't know why you would?

MR. MARKLEY: I don't have anything more than what we talked about yesterday briefly.

CHAIRMAN CERQUEIRA: Okay.

MR. MARKLEY: The process we went through with the ACRS when I used to be with them, the members of the existing committee could make nominations, but the main thing was that they all had to go through the same rigorous rating panel screening process so it's fair to everyone.

CHAIRMAN CERQUEIRA: We basically have gotten names submitted, and I think it's going through this outside review process right now. And I don't have any further information.

Could somebody look for Angela? I hope she realizes we decided, rather -- because somehow when the schedule got printed, there was an extra 15 minutes unaccounted for.

DR. ZELAC: If you'd like, I could go ahead -- this is Ron Zelac over here -- I could go ahead and give my presentation now.

CHAIRMAN CERQUEIRA: Yes, why don't we do that. Again I hate to do that because there may be sort of interested people, but "Question and Answer Process." All right, Ron?

I hope this is less controversial than your last one, which I thought was going to be straightforward. It's very unpredictable, you know, whatever issue will get someone's ire or anger some.

DR. ZELAC: This is the area relating to implementation of Part 35 that I've been directly involved with. Development of questions and answers. The objectives of this activity were to develop for agency-wide and public use standard answers to questions of general applicability.

And to, once having these standard answers for questions, post them on the NRC website for broad access on demand, both by our own staff as well as members of the public.

Where do the questions come from for which we are developing answers? Well, there were a series of agency/staff training sessions that preceded the implementation of the rule. Many questions came from those sessions, which involved both NRC personnel as well as state personnel.

We additionally had a series of public workshops on implementation of the revised rule before October. And again, many questions were developed. Some questions were answered on the spot at these meetings, and others were taken back for development of appropriate answers.

Additionally, we receive on a regular basis calls, e-mails, and letters from stakeholders on issues as they become more familiar with the specific

requirements under the rule.

And finally, implementation issues that are identified by NRC staff. There is a discussion on a bi-weekly teleconference of us here at headquarters, including the Offices of General Counsel and Enforcement, as well as ourselves and MSIB, with representatives from the four regional offices.

The process, which goes on for several slides, is as follows. The working group, which has been mentioned previously, develops draft answers for questions which have come to our attention.

IN some cases, the submitter of the question also suggests an answer. If that's the case, we look at it very carefully. If there is no answer, what the medical projects working group member and then the group itself reviews is a draft answer, appropriate rules sections, and a subject category.

The groups of draft questions and answers are then circulated throughout the agency, to the regions, to our Office of State and Tribal Programs, to the rule-making and guidance groups that have been involved in development of a lot of the guidance for the Part 35 rule. And we receive back comments, and make adjustments to these draft questions and answers as required.

After adjustments have been made, these draft questions and answers then go to our Office of General Counsel, which will provide additional input from a legal perspective in terms of the way these things are formulated.

Again, the idea is to develop a question and answer which will be usable, available by everyone at the agency when questions come in. If an individual licensee calls a region or calls headquarters, they should get the same answer to their particular queries. And they should have consistency across the country.

When the draft Q&A's come back from General Counsel, they are looked at by IMNS management, and occasionally further adjustments are made. If the adjustments are significant, this may involve re-review by the Office of General Counsel.

If the provider of the initial question had requested that the answers be sent to him or her directly, we do that, once we have a final answer to this particular question. If not, the final question and answer will then be posted on the NRC Part 35 website. And there is the address for it. That's the disadvantage of not having a podium where you can easily glance back at what's on the screen.

The current status of this Part 35 Q&A

process is that there are 78 final Q&A's that have been developed, and are posted on the website. And what I'll give to you, so you can kind of peruse it, if you haven't gone to the website previously.

There's a listing by subject category of those 78. And the second page of that hand-out is the first one on the list. So it gives you an example of what the format looks like in terms of the statement of the question, the provision of the answer, the indication of what the subject is, and availability of the rules sections that apply to that particular Q&A.

In addition to the 78 that are final and web-posted, we have another 168 which are in various stages of the review process; in the stream, and those are moving forward.

So we will have in the neighborhood, at the moment, of approximately 250. But this is a continuing process, because issues, as you all appreciate, do develop as the rule is more in use. And we will continue to answer those questions which come up through the implementation issues, develop from the bi-weekly teleconferences, as well as those that may come in from outside stakeholders.

CHAIRMAN CERQUEIRA: Thank you, Ron, and any questions for Ron?

DR. VETTER: Yes.

CHAIRMAN CERQUEIRA: Dick?

DR. VETTER: This is really quite good, and I expect that you'll eventually develop quite a long list of various questions and issues. And I don't know if you can answer this question or not, but how much of the regulated community knows that this exists?

And then perhaps how could we help you in getting the word out? Maybe through professional association newsletters or whatever.

DR. ZELAC: For those that are regulated, besides looking at the rule itself, there is the consolidated guidance document, 1556, Volume 9. And it, I think, may make mention of the fact -- it does make mention of the fact that it is listed and available on the website.

And if one reaches the website for that, they're close, if not at, the same place as this. This is very easily gotten to for anyone that's interested in it by simply going to the NRC public website, nrc.gov.

Clicking on the box dealing with nuclear materials, and very prominently is Part 35. When you click on that, then you get the whole series of things, and this is part of that.

SO those that are interested I think can

easily get to it. In terms of making that information known to people, I'm certainly open to suggestions. This is just part of what we're trying to make easily accessible to people who might have reason to need additional information above and beyond the rule itself, which of course is also posted on the web.

CHAIRMAN CERQUEIRA: I agree with Dick. This is very good and very useful, but it does need to be publicized to people. I would suggest that you contact the professional medical societies who have nominated people for this board, and just let them know about it.

They could probably just put a link on their websites to this, which I think would at least get this available to a broader number of --

DR. ZELAC: Good suggestion. Thank you very much.

CHAIRMAN CERQUEIRA: Thank you. Now Angela will talk about update recommendations from Fall 2003 meeting. And there is a tab.

MS. WILLIAMSON: Mr. Chairman, I'd like to begin by apologizing for not being here at 1:00. But from our previous discussion, I was under the impression that you were going to use the 1:00 to 1:50 time frame for some committee work on the commission briefing materials. So I guess I misunderstood the nature of our

conversation.

But to continue on, we're here at this point to discuss the recommendations from the October meeting. The October, 2002, meeting. And this shouldn't take much time.

So quickly, the first recommendation that ACMUI made was that -- that should say the ACMUI chairman. That's a typo in the memorandum, if you're looking at the memorandum.

It should say the ACMUI recommends that -- oh, no. I stand corrected. It's worded correctly. It says the ACMUI recommends that the chairman of ACMUI contact the NRC chairman to inquire about the status of the training and experience recommendations that you made to Part 35.

And of course this doesn't require any specific action by the NRC staff, and we reflected that in our response. So that one is pretty self-explanatory.

The second ACMUI recommendation is that the chairman of ACMUI form a standing subcommittee to review 35.1000 issues, and to recommend to the staff licensing guidance.

And that's a done deal, as you all know. That subcommittee has been formed. It was formed very shortly after the October 28 meeting.

Now, the next recommendation regarding sealed source model numbers as license conditions. Dr. Donna-Beth Howe of NRC staff actually gave you a presentation yesterday on this particular subject.

And she went into more detail than what is reflected here in our answer. But our official response to your recommendation that the NRC initiate a rule-making to modify Part 35 to override 10 CFR 30, Part 32 (g)(1) to allow a more generic listing of interstitial seeds and sources.

Well the staff believed that that rule-making was inappropriate, at least at this juncture. And as reflected in the answer, one reason why we believe that it wasn't appropriate is that we thought it would ultimately result in reduced source accountability, which would definitely undermine our mission of protecting the public health and safety.

And we further believe that given the political environment that we're in today, as a matter of fact as you well know we just went to -- we were just elevated to alert condition orange by the Office of Homeland Security.

And with there being such a sensitive political environment to any -- excuse me, a sensitive political environment regarding radioactive sources and

the threat of terrorism due to sources that are not accountable.

We just thought it would not sit well with members of Congress, or with the general public, if we made any overture that would even suggest reduced source accountability.

And from a practical standpoint, maybe that doesn't make much sense with your current experience with these types of sources, but perception is reality. And I think that if the public perceives that the NRC is reducing source accountability, it's just as well a done deal as far as they're concerned.

So we got your feedback yesterday on why you disagreed with this recommendation, but I do think it's important to take this time to underscore the fact that there are other interested parties whose views we have to take into consideration. And one of those parties, of course, is Congress. And we might have to very well answer to them in the future if we were to undertake this type of initiative.

So please keep that in mind.

DR. BRINKER: I recall from yesterday that one of the ways that was suggested to facilitate the licensees' paperwork was that they should ask for or request when they amend their license all of the marketed

-- for instance, this was in prostate seeds -- all of them, even if they had no intention of using them at the present time, nor stocking them.

Of course, when you do that, any utilization of that information for accountability purposes is negated since it has no real relationship to what the individual site has, or will even ever have.

So I understand your concerns, but it is just a perception. Perception can be false and misleading, as well as helpful.

MS. WILLIAMSON: I agree, but the general public is -- it tends to be inflexible with regard to anything related to radioactivity. And communicating that message to them is very difficult, because they don't seem to be terribly receptive to that type of response.

DR. WILLIAMSON: Well, then how do you explain the promulgation of a performance-based, less prescriptive rule. None of this makes any sense. In this one small case where the sources are orders of magnitude below the level of -- below the threshold of concern for these security measures we were discussing the other day.

I mean, this seems like really irrational. You could make the claim about the attempt to revise or

streamline any regulation. This is a general argument, and I guess I would like to see some evidence that the public is inflamed about the poor accountability of prostate brachytherapy sources.

CHAIRMAN CERQUEIRA: Jeff, I think this is, you know, if we look at our role in terms of protecting the public, patients, and radiation workers, the risks and everything are no greater whether it's one seed or another. But I think in today's environment, it's not going to change things.

I think Dr. Miller and Angela are aware of the fact that this committee feels that the risks, by allowing just kind of a generic listing, would be better. But I don't think we can change it at this point.

Ralph, did you have a comment?

MR. LIETO: Just two quick points. I think, based on yesterday, that Donna-Beth agreed that they were going to go back and look at this and come back to the committee.

But just I would like to make the point that I agree with you wholeheartedly on the accountability issue. I think we need to separate that from being authorized. I don't think anybody wants to decrease the accountability of the licensee for sealed sources.

I think what we're trying to do is reduce a

burden, both on the NRC staff at the regional level for amendments, as well as the licensee. And I think there might be some common ground where we can work on that by revisiting it, and coming back to the committee.

But I agree wholeheartedly, we don't want to reduce accountability.

MR. MARKLEY: We've definitely note the fact that you approved a motion yesterday to go back and look at how we might look at an alternative path, and focus on both licensee and regulatory burden.

DR. WILLIAMSON: And I think, you know, you have to distinguish between the perception of lack of accountability, and whether there really is lack of accountability.

And both the regulated community and the regulators have to, I think, stand up to the plate, and shouldn't fall back when there really is no risk. And I think I agree completely with Ralph. It seems to me that there are options to ensure that if NRC wants to track the source model, along with the number and their strength, that that could be done.

MR. MARKLEY: We agree, and finding what that right fit is is what we will be pursuing.

CHAIRMAN CERQUEIRA: Next item, Angela?

MS. WILLIAMSON: The final recommendation

that was made at the October 22 meeting was that the ACMUI recommended that NRC initiate the replacement process to replace three positions on the committee; that of nuclear cardiologist, patient advocate, and state representative.

The update to that action is that we have formed screening panels with members of -- with a non-NRC member that we refer to as an outside federal employee.

Briefly, the commission-directed rules here require that an outside employee, non-NRC but a federal employee, must help us in our determination as to whom we should recommend to them to replace members on the committee.

So we have identified those outside employees, and we have set up the screening panels. And two of them meet in June. And one, the patient advocate if I'm correct, if memory serves me correctly it's the patient advocate screening panel that meets in July.

So what will happen, at the conclusion of each of these panels, I will send up a commission paper and make a recommendation based upon obviously the person's credentials, but also upon the outside federal employee's comments regarding whom we should recommend.

So that's well underway. And hopefully we will have these persons identified by early fall, the

prospective replacements identified by early fall. So that by the -- at least by the next spring ACMUI session, those persons can be invited on the committee, and see how you conduct business. And then they will be full members, hopefully, by fall of 2004.

CHAIRMAN CERQUEIRA: I think that would be useful to have them attend at least one meeting of the full committee to kind of get a feel for the way things work.

And certainly it would be very critical to have them available for the Fall 2004 meeting. And I guess we'll have to monitor the progress and see how it's going.

Other questions for Angela? Okay. Making good progress here. The next item is "Part 35.1000 Licensing Guidance." Donna-Beth Howe and Robert Ayres.

DR. HOWE: I am going to be talking about the 35.1000 guidance, and how we got to where we got, and what our guidance is on the current things that we've identified under 35.1000.

And on the next slide -- and I'll be talking about half of it. I'll be talking about the microsphere brachytherapy sources and devices, the liquid brachytherapy sources and devices. And Bob Ayres will be talking about the intravascular brachytherapy.

What happens is we get a request in from a limited specific licensee. In many cases, we know the technology is out there ahead of time. We have a memorandum of understanding with the Food and Drug Administration, and we work very closely with them. Bob Ayres is on some of their advisory committees.

And we get information that we can share back and forth so we know what's coming down the pike. In many cases, our broad scope licensees are actually doing clinical studies with these devices. SO far they're devices. In anticipation either for a 510(k) at FDA, or a pre-market approval.

So we get to hear fairly early on what's out there. And when we end up with events, then we get to dig further in, and we hear more about what's happening with particular devices and get their characteristics and things.

At this point, all of our 1000 items are devices. And I think there's a reason for that, and I think it's because the therapeutic radiopharmaceuticals are written in a fairly loose manner so that almost any therapeutic radiopharmaceutical is going to fit into 35.300.

And I know you keep bringing up Zevlin. Zevlin fits right now directly in 35.300. There's no

question it is a therapeutic radiopharmaceutical. It is a radiopharmaceutical. And it fits directly in it. It's produced by manufacturers that are regulated under 32.72, which is the drug manufacturers, and handled by the radiopharmacies.

And so it's absolutely in 300 right now. Now, when we go to our final revised training and experience, there may be some issues with training and experience that may make people want to move it into 1000. But at this particular point, it's a 300 device. Okay?

Now, we looked at -- what we do is we look at the standard characteristics of a given product as it comes in. And we look at its unique characteristics. We look at unique safety problems that we have from a radiation safety perspective with NRC licensees.

So we're not getting involved in potential problems over on the FDA side. And we try to develop licensing guidance based on these.

We'll take the product. WE'll look at its standard characteristics, and we'll start on Part 35. And we'll go from 35 to the definitions, all the way to the last chapter. And we'll see if that product fits nicely into the regulations because we don't need to reinvent square wheels.

We have a document that shows how we are regulating different materials. It's gone through the review process. It's gone through the public process. WE look to see how well it fits into that process.

And then we take -- and so in many of the standard characteristics are going to fit perfectly. Some of the unique characteristics are going to make it not quite fit into the right box. And that's where we generally have to develop guidance. And then we also evaluate if we have medical events.

So let's start with the first one, which is going to be the microsphere brachytherapy sources. I know today people said that just because of the way manufacturers wanted to get this to market, it could go faster through the device regulations than the pharmaceutical regulations.

It's true it's faster through the device regulations, but the microspheres met the definition of a device. They did not meet the definition of a radiopharmaceutical.

So FDA brought them through the right center for their definitions, which is a deice. It does not have pharmacological activity, doesn't have physiological activity and biochemical reactivity.

So for the -- oh, I'm missing one of my

slides. So the standard characteristics are it is a sealed source. The yttrium is embedded in the glass matrix for the TheraSpheres. The yttrium 90 is permanently attached to the ionic spheres for the TheraSpheres.

It's used for permanent implant brachytherapy. Once it is embedded in the capillaries, it delivers its radiation dose. The materials don't move afterwards.

Then lets look at the unique characteristics. So we looked at the entire 35, and we said this fits right in 35.400. This was before we had 35.1000.

And we said, well, it really fits well, but there's some really unique characteristics. First of all, these are teeny tiny little sealed sources. They're not going to count them. You're not going to have a model number and a serial number.

And you use a very large number of them. So in this relationship, you're delivering hundreds of thousands of these at a time. And you have a special delivery system.

There's an argument this is a radiopharmaceutical. It doesn't go into solution. You're not injecting these the way you traditionally

would through either a syringe, or through an IV drip as you do with monoclonal antibodies.

Because what you have to do is you have to get these spheres up into suspension, and then deliver them into the body. And what we're finding out for our safety considerations are it is difficult to get these little beads up into suspension and into the body.

And originally when we looked at the sealed source and device review for the TheraSphere's microspheres, NRC did that review. And we did not include the delivery system. And it became very obvious -- from the very first Theraspheres used in the U.S. had a misadministration.

The second use of TheraSpheres in the U.S. had a misadministration. What was presented to the FDA was they had 10 years of experience in Canada, they delivered 98 percent of the spheres to the site. They had no problems. Our first two uses in the U.S. they couldn't deliver even 50 percent of the spheres into the body.

And so we started looking at root causes. And eventually it became very clear that the delivery system was critical to be able to administer these microspheres into the body.

And with TheraSpheres, they've done a number

of engineering changes to take some of the original Rube Goldberg mechanisms out. You had to put two needles into a vial with a V-point on the bottom. You had to agitate with saline coming through. Then you had to get it agitated enough to keep it in suspension, then run it through a long tube and into the person.

If you didn't align the needles correctly, then the spheres went in the wrong direction and back into the waste container. And you delivered 20 - 30 percent of what you were expected to deliver.

If you had holes in the septum, then the pressure in the system wasn't maintained. And so you may have spheres in the liquid shooting up into the air, causing potential contamination problems. And so Nordion has done a number of engineering corrections.

The other problem was do you even get these spheres into the body, and how do you know? Brachytherapy, you make measurements afterwards. Nordion put two radiation detection meters on so they could monitor the flow of the seeds into the body, and also monitor the flow of seeds back into the overflow valve. SO that they could get a real life measurement of whether things were going forward.

There was a pressure problem. They put a pressure syringe on. There was a spacer problem. So

they took care of those issues for us. There are still some more.

DR. NAG: Can you clarify that this is -- we are dealing with only the TheraSphere and not the Sirtex, which is similar, but yet dissimilar.

DR. HOWE: Right now I'm just talking about Nordion. Okay, then the TheraSphere -- and the other interesting part that's a unique characteristic is the TheraSpheres came through FDA in a humanitarian device exemption.

And what does that mean for us? We don't enforce NRC regulations, but it means that if it's used outside of the approval that FDA gave, it could be considered a research use. If it is a research use, then our licensees have to ensure that they are following 35.6, which is the protection of human research subjects.

So we're not enforcing FDA regulations. We're just making licensees aware that if they're off label for Theraspheres, then they may have to comply with additional NRC requirements. Okay?

So those are the safety things that we looked at.

DR. NAG: I might want to just add that when you're talking about the off-label, just for clarification, the TheraSphere was meant to be done for

the -- on the hepatic cell carcinoma, using it for liver meant that it was considered off-label.

DR. HOWE: Right. And so you'd have to go through 35.6. Now, the other thing is when TheraSpheres was first approved, they were for distinct amounts of material.

And what's happened as the product got out into the community is, instead of delivering everything to the liver, the practice of medicine has evolved the liver to one lobe. You consider how much radiation was given to the liver ahead of time, and you customize the prescription and the written directive to what's needed. So that's changing.

DR. WILLIAMSON: Could you clarify how the -- what quantity is prescribed when you say dose. Are you talking about activity, or are you talking about physical absorbed dose. And if so, how is it estimated a little bit, because this is where I think a little -- information to remind us of it would have been helpful.

DR. HOWE: Yes. It brings up another interesting point. With the TheraSpheres, you have different anatomies in the hepatic artery, and so you have to be careful about shunting.

So when we did the written directive, we looked at that and we said, well, the written directive

for the brachytherapy doesn't quite fit this. We have some unique problems.

It is the practice of medicine to decide that a certain amount of shunting to the lung is acceptable. So we're recommending that authorized users write a maximum dose that can be delivered to the lung.

So we don't end up with medical events every time something shunts, because that's a medical decision. So then we went back and we said for this particular device, putting so much activity in through the delivery system did not guarantee that activity was going to go to the site it needed to go to.

There could be shunting here. There could be other problems. So we based it on dose. And we're pretty much dependent on the physician's defining what they intend to deliver and assuring what it is.

DR. WILLIAMSON: It could be a physical based -- it could be actual absorbed dose inside the --

DR. HOWE: WE haven't specified.

DR. WILLIAMSON: Or it could be administered activity. It would be the authorized user's choice.

DR. HOWE: He has to confirm that whatever he is putting on a written directive is what he delivers within the limits that would trigger a medical event.

DR. NAG: Actually, you're not measuring the

dose, but on a practical point that will be done as amount to millicurie. And then you allow X percent, but usually up to 10 percent or 15 percent something to deliver. And the dose you get will depend on how much something there is to deliver.

So you really -- and I'm planning to give 10,000 centigray to the liver tumor because you really don't -- you don't have a way of measuring, unlike other brachytherapy where you can, you know, here are the sources, and --

DR. WILLIAMSON: You can use normal MERD dosimetry system, can't you, for this? And you do a pre-treatment study to estimate the uptake and the mass of the target organ and so on, and you make some sort of estimate I assume.

CHAIRMAN CERQUEIRA: David?

DR. DIAMOND: Donna-Beth, I've never used one of these in clinical practice. I've seen demonstrations. SO forgive me if this is inappropriate.

I'm almost approaching this as I would a patient with thyroid cancer in whom I'm about to deliver iodine 131. In that particular patient, I may know from an antecedent nuclear medicine uptake and scan that perhaps at 12 hours, the uptake to the thyroid is

whatever percent. Let's say 20, 30, 40, 50 percent.

And therefore, based upon that, what I'm prescribing in terms of millicurie, I have a reasonable expectation what the dose to the thyroid will actually be.

Is that -- I believe the analogy is somewhat valid here. You have a sense on your biodistribution studies what degree of shunting will occur. And perhaps just prescribed in terms of millicurie in terms of activity would be a useful way to rationalize this.

DR. HOWE: It's not quite the same. I mean, in this case, in I-131 --

DR. DIAMOND: And I know that one of the differences may be --

DR. HOWE: You get circulation --

DR. DIAMOND: One of the differences may be that it's not just a biodistribution based upon body physiology. There's a difference in biodistribution depending on catheter placement, the success of the localization in the hepatic artery or to the subsegments.

So I understand that's another variable involved which perhaps is the complicating feature.

DR. HOWE: And that is one of the complicating features that we have with us. And it

really is difficult to figure out what you've got going in there.

We didn't think activity alone was it. I'm looking forward to working with Lee, with your subcommittee to see if there's something better we can come up with.

That's bring up the point, we decided that the written directive needed to be modified to take care of shunting. We decided that the definition of "prescribed dose" needed to be revised for this particular material.

And then we got the SirSpheres. Now, the SirSpheres are different from the TheraSpheres. They deliver yttrium-90. The mechanism is pretty close to being the same. But the SirSpheres has a much smaller specific gravity.

And so these spheres stay up in solution longer. And there's actually a different technique in delivering them that may be appropriate for TheraSpheres too.

And that is that when they're being delivered, you still have this delivery system which is part of the sealed source and device registration. And you have stopped up so that you deliver a radiopaque dye inverse as you're delivering. Because what they're

finding out is that the microspheres go in and fill up the capillary bed. And once they fill up the capillary bed, you get backflow.

And that backflow can then go to places you don't want it to go. So our understanding is that, in addition to wanting to deliver a certain activity to the liver, there is a medical endpoint at which you end up with backflow of these spheres, you're not able to deliver any more yttrium spheres to the liver. And at that point, you terminate the treatment.

And we haven't brought this into the guidance yet, but what I'd like to bring into the guidance is that in the written directive, this concept of monitoring with fluoroscopy and making a medical endpoint that you can't put any more yttrium microspheres in is a part of the written directive.

So that when you find out that you can only put 30 percent of the spheres into this individual's liver, that's not a medical event. This is the most you can deliver. Because if you delivered the whole thing, with the backflow, you'd be sending it to the GI tract, and you'd be sending it over to the lungs.

DR. NAG: I think this is an important point, the difference between the TheraSphere and the SirSphere, that because of the different density of the

two microspheres, although they are very similar in size.

DR. HOWE: They're handled differently.

DR. NAG: The velocity will settle down. When you're injecting it, it will not always flow with the flow of your fluid, and can settle down earlier. And with the SirSphere, it will flow with the flow, and therefore get to the target, and therefore also it will fill up the target a lot faster.

DR. HOWE: Now the other thing is we've just had our first medical event with SirSpheres. They put -- We don't have the exact root cause, but it appears as if they put too many puncture wounds in the septum, and the pressure wasn't held on the delivery system.

And so the microspheres, the other advantage of SirSpheres visually is that they have a brown color so you can see whether they're going into the body. The TheraSpheres are a clear glass, and you can't necessarily see them.

So they realized they weren't getting the SirSpheres into the person. They only delivered maybe three percent. And so that was a medical event. So we do have unique characteristics for the two, and physicians are going to have to really pay attention to which one they're using, and use the right procedures for the right device.

And we're going to -- I think we're planning on writing an information notice on some of these technologies, just to make people aware they have to be aware of these small differences.

DR. DIAMOND: Donna, just as a general point, I think that the approach of incorporating a maximum allowable difference as far as shunting or what else is going on is very useful.

And as Doug and I are sitting here impolitely talking behind your back, we recognize that it is clearly impossible from the time of the antecedent dosimetric evaluation to the time of the actual therapeutic administration, which may only be a few minutes after, that minor differences in patient blood pressure, minor differences in patient hydration status, minor differences in the proximal-distal movement of that catheter by just a few millimeters can all substantially cause perturbations in the dose to the target, and reflux into the gastro-duodenal artery and so forth.

So I think the concept of allowing for this -- allowing for a maximum dose that would be acceptable to outside the primary site is useful. It would have been helpful to perhaps have a representative from industry, or someone who's actually used TheraSphere in a clinical setting before, because I don't think anyone

in this room has the direct experience.

DR. EGGLI: Having done liver infusion studies with other radiopharmaceuticals in the past, even if you change the infusion rate between the localization study and the therapeutic treatment, you will change the biodistribution of the material you're infusing.

DR. HOWE: There are all kinds of very subtle things that can change what's happening.

CHAIRMAN CERQUEIRA: Jeff?

DR. WILLIAMSON: Yes, I just want to remind everybody, I believe ACMUI had a discussion of this. And we had more supporting documentation at that time. And I think this was probably a preliminary to the development of the guidance that you have.

And I think at that time, the issue of whether a maximum amount of activity that could be taken up into the lungs should be put either in the prescription, or in the guidance limiting it.

And for the various reasons you mentioned, I believe the committee rejected that. And so I think it was --

DR. HOWE: I think I missed that ACMUI meeting. As I was developing this, I wanted to make sure that -- because I developed the guidance. I wanted to make sure that we were not getting medical events for

things that were within the scope of the practice of medicine.

DR. WILLIAMSON: Perhaps I've been misleading. Anyway, the -- I don't have a transcript. I'm going on the basis of my memory. But I think that the result -- the upshot of the discussion, consensus, was not to put prescriptive requirements in the guidance as to how much a physician could choose, intentionally or unintentionally, to deliver.

DR. HOWE: We're not saying that you can only -- we're saying the physician makes his own determination on how much, and if he puts it in the written directive. And he does get some shunting. He doesn't expect to get shunting, but he does get shunting, and it goes up to that level, then he's already made a decision in his practice of medicine. That's acceptable.

So we don't have --

DR. WILLIAMSON: This discussion was in the context of how closely should the NRC licensing guidance be patterned after the FDA approved product insert.

So the initial proposal was all these restrictive things should be put into the guidance, and that was of course changed.

DR. HOWE: And our concept is it's up to the doctor to put it in the written directive. If he doesn't

put it in the written directive and he gets shunting, he's going to have a medical event.

This is in his best interest to make a medical decision, and to include it in a written directive in the way he wants to write it, so that he does not have a medical event, when in fact there is an acceptable level that, in his mind, can move there without being in error.

Okay, we're trying to build in flexibility. And you'll see also with the GliaSite, we could end up with a medical event for every single one of these administrations if we do not realize that the written directive is a very key document for the doctor making his medical decision, and realizing what some of these unique properties are with these particular devices.

CHAIRMAN CERQUEIRA: I think it's a unique point, and we appreciate your willingness to work with us, but you have to look at this in the context of all the other things we do in medicine. You know, Dr. Brinker can prescribe beta blockers, nitrates, all kinds of medications that have a lot more risks to the patient, that he doesn't have to go through all this kind of, you know, regulation, I mean, or oversight. And I think here that you don't want to overdose people, but we don't want to be so narrow in the limits that we set that you're

going to impinge on the practice of medicine.

DR. HOWE: Well, as written directives are set up now, you just identify the target site. And so if you just identify the liver, and there's shunting and the doctor makes a medical decision he can live with, whatever amount of shunting he can go with. If all he's putting is the target site, he's now treated an unintended site. And so we're just trying to make sure that he writes what he wants to deliver in the manner he wants to deliver it.

DR. WILLIAMSON: Let me bring an analogy of another case.

CHAIRMAN CERQUEIRA: Dr. Nag.

DR. NAG: When we were doing the brachytherapy to the prostate, at the beginning, we had no idea that it would go into the lung say 15 years ago. And then after that we published that it can go to the lung. And in the medical directive it was that if you injected it into the site and it sent it to other place, or embolized to other places, that is not a misadministration. And you can do the same thing here, that you inject it to the liver and it sites in other areas.

DR. HOWE: But what you are doing is you are injecting into the prostate gland, and somehow it got

into the blood system and got carried to the lung. In this case, before it ever gets to the liver, it may be back flushed into another arterial system, and go to the lung or to the GI tract, so it's not that it got to where it was going, and then it moved afterwards. It's that it didn't get there. It went somewhere else in the process. It's not quite the same thing.

DR. NAG: It is, because when you're implanting into the prostate, you're implanting into a blood vessel. And the ones that went into the blood vessel goes into the lung. I mean, so it must be the same thing.

CHAIRMAN CERQUEIRA: It's the same situation --

DR. NAG: Very similar situation. I think, you know, this is not a mistake on the part of the physician, you know, it shouldn't become a misadministration. That's the normal way it goes. The normal way blood flows is into the liver, and then come up the shunt into other organs. But the other thing I wanted to add, when you -- when this physician knows that the, you know, misadministration or the medical event you are describing, when he saw that the steroids were flowing to other sites, he stopped. That is the right thing to do. That's not misadministration. Can you go

into a little more detail?

DR. HOWE: You have to be careful. A medical event is a medical event because an error happened. It does not say that there is damage to the patient. It does not say that you did not take the proper medical care to stop the administration. It needs to be reported so that we can do trends, we can follow-up. Otherwise, we would not be as involved as we are with monitoring what's happening with the SIRSpheres as they're continuing to evolve engineering improvements for the delivery system. And it looks like we'll probably be involved in engineering -- the State of Massachusetts will be involved in engineering improvements to the delivery system for the SIRSpheres. A medical event doesn't mean we harm the patient. It means something went wrong with the administration, and it wasn't given as intended. And then what we do with that is generally more of an information thing. We don't -- it's not -- you were talking this morning about statistics. The statistics are low and they really don't mean anything because the numbers are so low. But we may put out an information notice that makes licensees aware of some of the problems.

DR. NAG: But unfortunately, once you report the medical event, whether intended or unintended, at

first consequence, you know, it becomes like immediate reflex, there's a medical event; therefore, something must be wrong. And, therefore, you know, you're going to a penalty and --

DR. HOWE: What you saw with Roberto this morning is that there are many, many medical events where there is no violation. Medical events are not violations. There may be other things that are related that are caused by this, but a medical event is not a violation.

CHAIRMAN CERQUEIRA: But a medical event is something we need to track and identify. And what we're telling you is that in the practice of medicine, this does not constitute, you know, danger to the patient or to the public.

Now, Doug, you had a comment to make?

DR. EGGLI: Yeah. From someone who hopes to be a provider of this service, I don't have a problem specifying a percentage of the administered activity that I will allow to go to the lung, or allow to go to the GI tract. In fact, if you use a 20-micron sphere, about 10 percent that hits the lung is going to pass into the systemic circuit anyway. There's a lot of collateral exposure with these things. And, you know, if I'm going to do this, I don't have a problem saying I will allow 10

percent of the dose to hit the lung, or whatever we determine the radiation burden is. I'm actually more worried about the GI tract than I am about the lung, because a whole pile of this stuff is going to end up in the gastroduodenaladian, and it's going to radiate the bejeebers out of the antrum. And I actually worry more about the stomach than I do about the lung. But again, I don't have a problem in a written directive specifying that it is my intent not to go beyond this limit. So to me, that's not a problem at all, as a person who hopes to be an end-user of this.

CHAIRMAN CERQUEIRA: Ruth, and then Jeff.

DR. WILLIAMSON: Well, I think maybe --

CHAIRMAN CERQUEIRA: Wait, Jeff.

DR. WILLIAMSON: Sorry.

CHAIRMAN CERQUEIRA: Ruth first.

MS. McBURNEY: Well, I think that it's not for us to try to redefine what medical event is at this meeting. It's to try to figure out how this licensing guidance can achieve not having a lot of medical events that are not truly medical events. And I think that's what Donna-Beth is trying to say.

DR. HOWE: That's exactly what we're trying to do.

DR. WILLIAMSON: Okay. Well, I guess, you

know, what I'm hearing is, you know, there's no certain amount of controversy, and that's because I think you're patterning the licensing guide after a brachytherapy mode of delivery where the ability to specify where you put the sources is more under control of the authorized user. And there is a component of this that's almost like a systemic or regional radiopharmaceutical treatment, so I think, you know, you could interpret perhaps part of what we were saying earlier today as to, you know, be careful in pushing the brachytherapy model of treatment planning and delivery for this, because if you do, you'll get in trouble. You know, so I suppose if Dr. Eggli said I want no more than 10 percent to the lung, and he got 12 and a half percent, would he have to report that as a misadministration? What would exactly the criterion be? Or would he be able to revise it and say okay, I accept 12 and a half percent because the sources haven't completely decayed?

DR. EGGLI: What I'm probably going to do is look at a level where I think that we're going to get pulmonary toxicity and set that as my level. And, in fact, if I exceed that, I probably need to report that if I'm going to get pulmonary toxicity out of the treatment.

DR. HOWE: And that's kind of what we expect the physicians to be doing normally. Okay? If I can go

on to the next, our safety problems. We had many misadministrations because you couldn't deliver it. There is the spread of removal contamination, so your radiation safety officer needs to be aware, and you need to monitor for these things. Shunting is common. Okay. And that's a medical decision. Anything else? Oh, and then SIRSpheres, we believe that there's probably going to be a different treatment end-point that needs to be identified in the written directive, because it's going to be a medical end-point, and physicians will use it. And it's the right thing to do, and we just want to avoid having things reported that don't need to be reported. Okay?

So the next one is going to be the liquid brachytherapy sources and devices. Once again, this particular liquid source is not a radiopharmaceutical. It is not a drug. It came through the Device Center. It is a device. It's Iotrex. It comes in the GliaSite radiation therapy system. When it went through the Sealed Source and Device Registry, there were engineering questions that were answered and evaluated in the compatibility between the device and the catheters. And one of the things you would see in our guidance is that these are for very specific products. If you change the -- a different microsphere, you change a different liquid

I-125, this is not an approval for any liquid I-125. You change that, and you're a broad scope licensee, we expect you to do a safety evaluation. If you're a limited-specific licensee, you have to come in for an amendment. Okay?

And one of the other problems that you have with this I-125 is that there is a disassociation between the I-125 and the molecule that it is attached to. And once it disassociates, you end up with the I-125 going through the catheter membrane, and into the body.

Now we cannot enforce FDA labeling, and we don't. FDA labeling says that you'll block the thyroid. It may be a practice of medicine not to block the thyroid. It only takes a small amount of I-125 to throw you into a medical event, so you want to keep that in mind. But we don't require you to block the thyroid. We don't say anything about that. But we know there is this amount of I-125 that will disassociate across and go into the person. So if we use the strict definition of a leaking source - this is a contained source - if we use the strict definition of a leaking source at .0005 micro curies, every single administration with a glucide would probably be a leaking source report. We don't want to have these reported as leaking sources, because we know there's a certain amount going across. What we want to

see as a leaking source report is a true failure of the catheter to contain the source, and so we're trying to put that into our guidance and bring home to people this is a unique property of this particular device, and we want to incorporate that.

Okay. It is an I-125 source. It is a temporary implant. Next one. Okay. So it's unique characteristics are -- this is our first liquid contained source. It has a special containment system. The I-125 liquid and the catheter are compatible. We can't make any judgments about any other catheters, any other I- 125 liquid. That's why broad scope has to do its safety evaluation, and limited-specific has to come in for an amendment, so we could get a chance to review.

You have an earlier surgical implant of the containment system, so you can't test for leakage out on the benchtop. The system is in. We believe that you can test for leakage for this balloon in the normal practice, because they image the balloon to make sure it's in the right place. They have saline or normally they'll put a radiopaque dye into it.

First use of the glucide was a misadministration. Why? Because they did have their syringes labeled. You use a small amount of I-125. You bring it up to volume with 10 cc's of saline. You use 10

cc's of radiopaque dye to image the balloon before you put the I-125 in. The procedures were put the radiopaque dye in, pull it out, put the iodine in, put the same volume, 10 cc's of saline in. They picked up the wrong syringe. They put the radiopaque dye in. There was self-absorption. Only about 30 percent of the dose that should have been delivered to the brain tissue was delivered.

We originally said okay, this is the only sealed source we have that has self-absorption problems in the delivery system, so we were going to require people to, when they remove the Iotrex from the balloon at the end of the procedure, to make a radiation measurement to ensure that they had delivered what they intended to deliver dose-wise.

The manufacturer and some of our licensees came in and said that's too much of a burden on us. We'd like to have a volumetric test.

DR. WILLIAMSON: Can you explain radiation measurement? I'm not sure I understand what you're expecting them to do.

DR. HOWE: We were expecting them, as they pull the liquid out, put the syringe back into a dose calibrated, and make at least enough of a measurement to know that it's not going to be 20 percent off. It ends

up the manufacturer did not want licensees to have to do that, so they came in with an alternative. They said we've done tests, that if we dilute the radiopaque dye, the specific dye down to 25 percent volume, it's sufficient to image the balloon before you put it in, make sure the balloon is in tact. And if we make a mistake, and we take it out and we end up putting it back in, it will not result in 20 percent of the dye being absorbed, so you won't have a medical event.

DR. WILLIAMSON: I see. So what you're suggesting is that as a way to determine whether they have mistakenly put the radiopaque dye in with the radioactive solution, when you withdraw it --

DR. HOWE: You do a measurement.

DR. WILLIAMSON: Measure it. I see, and then if it were there, you'd see the effects of self --

DR. HOWE: Yes.

DR. WILLIAMSON: You would never know though whether the short, the gap in expected versus measured was due to leaving some of the fluid inside the balloon and delivery system versus self- absorption.

DR. HOWE: If it ends up with the flushing, at the flushing system, you get almost all the fluid back out. This was not a borderline. This was like 60 to 70 percent of the dose was absorbed by the radiopaque dye.

Now the concept is, if you use a dilute dye, even if you put the dye back in, you'll absorb less than 20 percent of the dose, and you may not deliver what you had expected to deliver, but you have not triggered NRC's medical event reporting. And so we have accepted that, and you'll see that in the guidance. But it's really tied into following the manufacturer's instructions on the radiopaque dye, because we bought into that as a method of proof that you have at least not gotten a medical event. Am I clear?

DR. DIAMOND: Just as someone who's also used this technique, just to give you a little context. The purpose of instilling this dye is to make sure that you're in the right place, and that the balloon is in tact. You should know, of course, how much dye you've instilled; therefore, you should know exactly how much you should get out.

DR. HOWE: It ends up both volumes of that and the saline are pretty similar.

DR. DIAMOND: Right. So just with that simple knowledge, you know a priori that you should not have a problem with self- absorption because an excessive amount of dye remaining within that balloon. So as long as one follows the letter of procedure, it really is not an issue, and an easily solvable problem, or avoidable

problem.

DR. HOWE: And the other thing the manufacturer has done, is they've really recommended very strongly, and I think they've included labels so that people now can label the syringes, and try to cut down on the human factors problems.

DR. NAG: Yeah, I think those things are very important. However, one thing that is -- that we haven't addressed at NRC and all the medical community, and that is what dose is required. Now we are calling something 20 percent more or less than what we intend to be a medical event, but we have no idea what dose to give. So, you know, you may want to give 10,000, you may want to give 20,000 --

DR. HOWE: That's the practice of medicine.

DR. DIAMOND: That'S the practice of medicine, and to treat these patients --

DR. HOWE: But if you decide to give 2,000, and you measure before you go in an amount you think is going to give 2,000, and then -- that's okay.

DR. NAG: Right. But it's --

DR. HOWE: It's the practice of medicine.

DR. DIAMOND: But Subir's point is not really germane. We have no idea at this point with technology what is the optimal and so forth, and that

really is not germane to this discussion.

DR. HOWE: That's the practice of medicine.

DR. NAG: You may but the thing is we are now calling something a medical event when we don't know what dose to give, so we may have a medical event, and we may have no problems.

DR. HOWE: No, no, no, no. If you decide to give a certain dose, and you measure the activity to give that dose, what we're trying to do with the radiopaque dye part is assure that the activity you put in will deliver whatever dose you wanted it to be. We're not saying what the dose is. And if you dilute the radiopaque dye in a certain manner, that you're guaranteed that it will not self-absorb more than 20 percent. So you may be off in what you want to give, but you haven't triggered the medical event yet.

DR. WILLIAMSON: And medical event is sort of an arbitrary regulatory end-point. And there are, you know, many procedures maybe where we don't know the optimal absorbed dose within 20 percent, but the point is, it's -- a physician at some point specifies this is how much I want to give, either centigray or millicuries, and there's a system for allowing you so much deviation from the written prescriptions. You know, uncertainty biologically has nothing to do with it.

DR. HOWE: And that's kind of an overview of where we got to with the guidance, and with the GliaSite too. We looked at it and we said gee, this is a liquid source. It's a brachytherapy. It fit brachytherapy really nicely except for some of the things that were really specific to sealed sources. And so for those things that were specific to sealed sources, we made slight tweaks in the guidance so that it would be applicable to a liquid or a contained source, leak testing is a good example.

MR. LIETO: I just wanted just a quick question. You're not saying that this is a sealed source device. Did you say it was?

DR. HOWE: We're saying it's a liquid brachytherapy source, and it's a contained source. We're not saying it's a sealed source, but it comes under sealed sources and devices. It's a device, and so we put it in the registry.

CHAIRMAN CERQUEIRA: We have a comment from the audience.

DR. HEVEZI: Yeah. Jim Hevezi, representing ASTRO, who were involved in the sanitonial and the clinical trials for this device. And I remember that we had to monitor urine levels about liquid iodine, and apparently in the current application, that requirement

is no longer there to monitor urine levels. Is that correct?

DR. HOWE: Monitoring urine levels was probably in the clinical trials to support the 510(k). NRC does not enforce FDA labeling, or FDA requirements. And so if the labeling says monitor urine, we recognize in practice of medicine certain physicians aren't going to monitor.

DR. DIAMOND: The answer is we don't.

DR. HOWE: And so it's not a requirement for us, and it has never been a requirement for us.

DR. HEVEZI: I understand that. If the balloon leaks after these initial tests though, how will you know that?

DR. HOWE: If it's a catastrophic loss, then the volumetric measurement, you measure -- the manufacturer has essentially gotten us to accept the idea that if you measure the volume of material coming out, and it's the same as the volume of the material you put in, there is an assumption that you have --

DR. HEVEZI: An intact balloon.

DR. HOWE: You have an intact balloon.

DR. HEVEZI: Okay. But if not?

DR. HOWE: And nothing precludes you from doing a different measure.

DR. HEVEZI: Okay.

DR. HOWE: And you should be, for a temporary implant, you're supposed to do a survey of the patient after the material is removed. If it's gross, you'd see.

DR. HEVEZI: Thank you.

CHAIRMAN CERQUEIRA: Jeff had a question.

DR. WILLIAMSON: Oh, I just want to make a general comment. I was involved actually as a contractor and consultant for the company when they developed it, and helped put together and, you know, create the system of calibration, and dose specification. And I think, you know, clearly the intent is, it is a brachytherapy-like device. It relies on correct surgical positioning of it, verification by imaging, surface dose, distant from the surface-based dose specification using absorbed dose, and not activity. And, you know, much closer to a conventional radiotherapy planning system than, you know, typical nuclear medicine.

CHAIRMAN CERQUEIRA: Thank you. Well, I guess -- Bob. I forgot Bob. Okay.

DR. AYRES: Well, based on my earlier presentation, I don't think I have a ghost of a chance of doing this one in 15 minutes, but we'll give it a shot. I'm talking about one at least that's been talked about

quite a bit, and that's the intravascular brachytherapy. And we deem that to be a new technology that's not covered by either 35.400 manual brachytherapy or 35.600 high dose rate, or low or medium, whatever, remote afterloading brachytherapy.

Also, these IVB devices do deliver high dose rates, and that's imparting to our Part 35 definition of greater than 12 gray at the prescription point. All of them do. Let's see, I didn't get the -- oh, next slide then.

The conditions of use in our guidance which is on our website as was the therapies that Donna-Beth talked about, are limited only to intravascular brachytherapy, which is far broader than the FDA label use, so an awful lot of what -- a considerable amount of what is done, is done what would be FDA off-label. And we require these procedures to be conducted under the supervision of an authorized user. And the authorized user is to consult with the interventional cardiologist and the medical physicist in the treatment planning part of these. And we require, in this case, the physical presence of the authorized user, or the authorized medical physicist. These additional requirements really are what allows us to authorize wider use, because of the medical expertise in both the medical physicist and the

authorized user in doing treatments outside of the approved FDA uses. Next slide.

The training and experience that authorized users - I kind of mixed things up there - are really 35.600 and 400 uses. I've got one citation to the new -- to 600, and the other one is in Subpart J, but it's either 35.940 or 35.490, 35.690 or 35.960. With having two sets of training and experience requirements makes things a little more complicated now. That's been discussed, I think, already.

We require vendor training for the authorized user and the medical physicist, and for the interventional cardiologist. One of the things that this one, and it's disturbing to me. I have now collected essentially 100 medical events related to these systems over the past several years, which is far and above what we see with almost any other modality. And almost of them, 90 belong to one vendor. I'm planning on writing this up as sort of my parting gift to management before I leave, with some suggestions that we do need to increase some of our requirements here.

So where relevant, I put these arrows in the particular sections that go along with the requirement. I will say, of the 100, only about 40 or 50 are out of NMED database that are reportable to NRC. The other is

out of the corresponding MAUD database at FDA, and include things that wouldn't be reported to us, but have some issues, like damage to the catheter, slitting catheters or tearing the ends off of, which you could take it together with our reported lost control of sources, presents the scenario for the worst case -- presents an opportunity for the worst case scenario, which is sources getting outside of containment and loose in the vasculature. So we have the -- we require the medical physicist to perform an independent measurement of source output.

In my collection over the past several years, we've had 11 vendor calibration errors reported by our licensees. Next slide. The written directive prior to treatment specifies the treatment site, the radionuclide in adults, the same written directive requirements for high dose rate and remote afterload.

We require written emergency procedures. In other words, you're prepared if it happens for stuck sources. We have 28 events reported where sources have been stuck in the vasculature, and they've had to go to bailout procedures or other alternative techniques to get those out. And detached sources. We've had no reports on those. And the standard brachytherapy radiation safety precaution --

DR. WILLIAMSON: There have been sources that actually have escaped the containment catheter and gotten lodged independently in the vasculature --

DR. AYRES: No, no, no, no. I said you put two events together, fortunately that haven't happened together that I'm aware of, we have slit catheters and ends torn off catheters, and we've had sources loose in the catheter system, but not outside of it. But if the two ever happened together, that could be a bad day.

The standard brachytherapy precaution protection for patients, members of the public, medical personnel and everybody - and you all recall the Pennsylvania incident, was survey the patient after a brachytherapy treatment, and make sure that you've left nothing in there. Next slide.

Those were general conditions that apply to all three presently approved systems, which are Cordis, Novoste, and Guidant. And then we have specific conditions, because each of these are of a unique design that apply to a particular vendor's intervascular brachytherapy. The first one for Cordis is don't use after the expiration date. That expiration date is set in the SS&D. That's a point where the radiation damage to the nylon ribbon embrittles it to the extent that it could break.

Source stepping is permitted, provided you've worked out a technique. Don't try it off-the-cuff so to speak. The vendors, and this is the thing that goes with FDA approved and not FDA approved. The FDA guidance, an exception to the guidance system has not approved stepping, so they do not allow the vendors to develop techniques and advertise such a use, which puts the entire burden on the licensee if they're going to do an off-label use of a device. And so we're just saying work it out, develop appropriate procedures and follow those.

A reminder to submit calculations or measurements demonstrating Part 20 compliance requirements. These sources have enough radiation that you may exceed the occupational or unrestricted area radiation limits, and you may need to consider shielding. We don't go so far as to say you're going to require a shielded room with interlocks or anything like that. They're sort of intermediate between a high dose rate, load afterloader, and manual brachytherapy and the amount of radiation emitted. Particularly when you get up to the larger seed ribbons of 14 seeds or so, you get up around 600 millicuries of Iridium there. And they approved a 35 millicurie per seed of maximum activity in ribbons of 6, 10, or 14 seeds. And that's just the

approval there.

Next slide. The Novoste-specific conditions. The use of the introducer sheaths are less contraindicated for the individual patient. We've had some licensees that say they're contraindicated for all my patients, and then they have a misadministration. That's one of the things I want to see changed. This is where we have a lot of events. In fact, it was one of our very first events with intravascular brachytherapy system. The sources have been -- we've had reports of sources blocked 15 times on return after treatment, and it's usually due to crimping the catheter at the entry valve, and 11 on source introduction. Insertion, you say well, that wouldn't be a medical event. Well, it usually is because part of the source is getting out, not all of it, so they do place sources in the wrong place.

The use of a dual syringe system. We've had two events that have been reported. If you run out of fluid, the source free- float and they sink to the lowest point in the vasculature, which is probably somewhere in the abdominal area, but it's certainly not the treatment site.

We also -- same thing. The FDA has not approved source stepping for this system, and so we remind our licensees that they need to have appropriate

procedures if they're going to do that. Next slide.

We encourage locked storage of the device. It's something that could easily be picked up. It's a hand-held little unit about that big, and come up with loss of control of the sources and get outside of the control, so simply security of the radioactive material. And the function depends on an appropriate inspection, and service intervals, so we simply require that they be inspected and serviced at the manufacturer's recommended intervals. And we tend to ensure that by causing the device to lock-down after so many transients of the source. And this particular device is battery operated. The battery has a limited life too. And then the usual line item for activity of the sources, and the total, and there's now about 6 different models of these things, all with different source train links, whether it's a five French or a three and a half French catheter. There's those two variants, and then there's also what they call the Corona system which uses a carbon dioxide inflated centering balloon because they're using these to treat the large leg peripheral arteries, such as the popliteal arteries or the femoral artery. And that particular application is clinical trials only at this point.

Reminder that source separation during treatment are to be reported as possible medical events.

If you're trying to treat one site, and your source has ripped all apart, well obviously, you're not giving the radiation treatment that you intended to do. This would be observed on fluoroscopy. You can't really see these little Strontium sources on fluoroscopy. You can usually see them on sign afterwards when you look at it, but you can't tell if you get a significant separation in your gold markers.

DR. DIAMOND: That's exactly right. It's a moot point, because if you could see both the gold marker then, of course, the sources are together.

DR. AYRES: That's true. I mean, there's no -- what I was just simply trying to say, there are not direct -- you don't directly visualize the source separation. You visualize an indication of that of the gold marker links increasing, the distance between.

DR. NAG: Bob, you had mentioned that one of these devices that had the majority of the medical events --

DR. AYRES: You're looking at it, 89. And you kind of see that by the numbers on the individual problem areas. I mean, the FDA, and I discounted an awful lot of them because they have no radiation consequences. I only included their reports out of the MAUD database, such as, as I said, the damaged catheters,

the gold markers being moved substantially which would be a potential positioning problem. The two patients deaths I listed also, whether they were due or not due to this treatment. Without a post mortem there was no way to tell, so -- but they obviously were of sufficient interest to the licensee or the medical institution reported them to the FDA.

Okay. Next slide. With the Guidant, that's a source -- uses a source assembly changeable cartridge, and the manufacturer limits that to 60 days or in 650 cycles, and that's part of the SS&D. And so SS&D limitations are normally incorporated in the licensing. And that relates to -- the 60 days relates to half- life. It's P-32, and the 650 cycles is a design limit for reliability-related design limit.

Again, a locked storage device and a console control key, just to protect the materials. And again, this is a mechanical -- this is more like a traditional wire-driven HDR, that the device be inspected and serviced. I left the D off - at manufacturer recommended intervals. Next slide.

600 millicuries per source assembly, two source assemblies per device. In other words, we always allow for the one you're using and the exchange one to be there. Daily system checks. This very much mimics the

HDR. The device is very much -- I mean, it is a specialized HDR, so most of the HDR safety checks were pertinent, such as the proper operational check of the console and the indicator lamps, source status indicators, visually checking the catheters and connectors, and periodically checking the source position accuracy. Next slide.

CHAIRMAN CERQUEIRA: Bob, we've got a question from the audience.

DR. AYRES: Yeah.

CHAIRMAN CERQUEIRA: From Jeff, I think.

DR. WILLIAMSON: All right. For this system, do you still use the 35.400 training and experience criteria for the physician?

DR. AYRES: 600.

DR. WILLIAMSON: 600. You use 600.

DR. AYRES: Uh-huh.

DR. WILLIAMSON: Okay. And then for the AMP, you would expect them to have the --

DR. AYRES: HDR.

DR. WILLIAMSON: HDR AMP, as opposed to a teletherapy or something --

DR. AYRES: Yeah. I mean, it's directly pertinent to the -- particularly -- this one in particular.

DR. WILLIAMSON: Yeah. I thought you mentioned initially --

DR. AYRES: Well, the 400 applies to the Cordis.

DR. WILLIAMSON: Okay. I see.

DR. AYRES: And the 600 applies to the Novoste and the Guidant.

DR. WILLIAMSON: All right.

DR. AYRES: At source exchange, you would expect the usual things, the source uniformity. In this case, it's not a tiny little source. It treats, I think, 30 millimeters.

DR. NAG: 20 millimeters.

DR. AYRES: 20. It's a long source. And just that it's uniform over its link. Source positioning accuracy, battery back-up. You know, that's what bails you out when you have lightning hits your institution and knocks out the power. Source transient time, and timer accuracy and linearity.

In this case, stepping and pull-back procedures have been established and approved by the FDA, and we don't -- and following, you know, the manufacturer's procedures for this should be adequate. We had a couple of misadministrations that related to training, the way the source is positioned with the new

-- it's a slight model change to go to the stepping procedure. And it has a different positioning method. It just doesn't run the wire out. You've got to then jog it into position. And there were some training errors in this, and they didn't do that, and they treated in the wrong place. That's a training issue.

DR. WILLIAMSON: I've got one more maybe relatively minor question. You know, in 35.600 calibration of the source or verification of the calibration of the source by the user is a central requirement, so do you expect that for this?

DR. AYRES: Yeah. That was one of the generic that applied to all three systems.

DR. WILLIAMSON: Okay. Could you expand upon a little bit about as to what sorts of procedure you expect?

DR. AYRES: Well, yeah. It would be even pretty much along the lines of calibrating any other HDR source, although the measurement instrument could be different. You could use a traditional dose calibrator, except what's required is that it go to a calibration laboratory, an ADCL and be calibrated with an appropriate positioning device for the sources which you're measuring, be they -- in other words, if you're using all three, you would need to have Wisconsin say, calibrate

your measurement chamber for Strontium 90, Novoste seeds, Iridium 192, Cordis ribbons, and Guidant wire P-32 source.

DR. WILLIAMSON: Does the ADCL offer P-32 calibration certs?

DR. AYRES: Yes. The last I knew, they did. Yeah. It's usually a -- it's a component of the FDA approval, that there be appropriate calibration procedure provided. And I mentioned, we had - I forget the number now - a number of these. And some of them were true calibration errors, and some of them were calculations. Some vendors supply the activity in both seconds, and minutes and seconds. They convert it to that for the treatment time as a function of vessel diameter radius, which is another issue. One vendor uses radius, one uses diameter. Users have confused those and got 100 percent overdoses, because they used radius where they should have used diameter. It's Cordis and Novoste that uses two different values for calculating the dose.

Anyway, some of the calibration errors were so simple that they couldn't convert seconds to minutes and seconds. They made errors. Others were true measurement errors.

MR. LIETO: Bob, was that with the Guidant?

DR. AYRES: No, that was with Novoste. Next

slide. I may be actually pretty well close to on time there. Yes.

CHAIRMAN CERQUEIRA: Ruth.

MS. McBURNEY: Could we get copies of your slides? I don't think they were included.

DR. AYRES: Yeah. I was a little late on those because I was busy trying to --

MS. McBURNEY: I think it would be important to our subcommittee's discussions.

DR. AYRES: I think Angela said she'd take care of that.

MS. McBURNEY: Okay.

CHAIRMAN CERQUEIRA: Do you need them for your subcommittee meeting?

MS. McBURNEY: Well, I think it would be helpful.

DR. AYRES: Well, I've got one set I brought with me. I'll hand them to you on my way out. Yes.

MR. LIETO: Bob, how many of these errors and events have occurred since the guidance went into -- I think it's been in place for a little bit over a year now.

DR. AYRES: Okay. It's kind of --

MR. LIETO: Do you have like a breakdown or have a general feeling as to a lot of these were before,

and not so many now?

DR. AYRES: I happened to bring my talk on that that I had given at brachytherapy meetings, and I can -- Novoste had a -- and this was as of first year, Novoste 89, Cordis 12, Guidant 10. That's totals. I have broken down that after approval by the FDA, which all occurred in late `99, as I recall. Don't hold me to that, but that's what my memory serves me. Novoste had 77, Guidant 5, and Cordis 12. Now the interesting thing though, you look into them a little more deeply. Almost all the Novoste are device-related/human factor/design. The Guidant, Galileo, and the Cordis Checkmate, a lot of them are really dumb. Okay?

The Cordis Checkmate ones are tripping over ribbons, and pulling them out of the shield, and stepping on them, or walking away and not having it hooked on the hand, and pulling it out, and then getting a room away and noticing they're holding the whole ribbon in the hand sort of thing. It's pretty hard to be device-related with a nylon ribbon of Iridium sources you push through a shield into the catheter.

The other new issue that we're starting, and we had two by one of the leading physicians that are -- that led all of the work on developing this just recently, and so it looks like we're running into severe

problems with the new three and a half French catheter on the Novoste system. It's so flexible, it kinks easily, and we get blocked sources on entry. And in one case, they went the whole treatment time, thought they saw the markers. They were really looking for markers on the catheter, not the source markers.

DR. EGGLI: Do you know if the Novoste incidents are out of proportion to the market share that Novoste has?

DR. AYRES: I would certainly think so considering the number. The other thing is, it's clear there's almost no incident of the other two that are related to the device, failure or design. You see -- we've had these training issues I mentioned on Guidant. Another one, early-on they had a 90 degree elbow that they connected the treatment catheter to, and then they eliminated that. And they had the trainer right there at the same time with a new longer catheter. They put the new longer catheter on, and still put the elbow on, and treated 35 centimeters from the intended treatment site.

The only mechanical design issue I'm seeing on the Guidant system is that it appears that the dummy source that runs in, and the hot source have exactly the same trip threshold, so they sometimes -- there have been several occasions where they've been able to successfully

run in the dummy source, and then get multiple retractions and tries that the active source retracts because of resistance. It's because there's just no difference between, threshold difference between the force sensor on the dummy source, and the force sensor on the active source.

DR. NAG: I didn't get that. If they're the same then -- I didn't get that. If they're the same, then if the dummy goes in, the real one should go in as well.

DR. AYRES: Yeah. Plus or minus whatever uncertainty there is in each run in that you have, and any variations in manufacture. I suggested that simple way to do that would be to make the dummy source slightly larger, just slightly --

DR. WILLIAMSON: I see. So that the dummy source is a more conservative --

DR. AYRES: More conservative, which is supposed to be, and it is not.

CHAIRMAN CERQUEIRA: There's a question from the audience.

DR. AYRES: Yes.

PARTICIPANT: Just a comment. I mean, there's a valve called the Touhey valve, that if it's not properly opened for source insertion and removal, that

you'll have a stick. Are a lot of these counted as the events that you are describing?

DR. AYRES: Almost all of the stuck sources going in and out, and it's a complex issue in one sense. If you over-tighten it, you block the sources. But if you over-tighten it too far, even if you loosen it, the sources are still blocked because the plastic catheter has a memory, and it doesn't return -- I'm trying to think of the word.

DR. WILLIAMSON: Yeah, they stick at the --

DR. AYRES: Yeah. The catheter doesn't rebound to its original diameter, and it takes time for that plastic to relax and the blockage --

DR. WILLIAMSON: I think at Washington University, we were one of the first to discover this, and we couldn't understand why --

DR. AYRES: I didn't know whether you wanted the credit for that or not, but I will say that Dr. Williamson did an excellent root cause analysis when they had their's. And, in fact, several of his institution's recommendations are in this guidance, based on the very first incident we had.

CHAIRMAN CERQUEIRA: Dr. Nag.

DR. NAG: Yeah. We had this now under .1000. Now at what point does the emerging technology

become a -- like with new technology, for example, one that is basically the same as the HDR afterloader, at what point, or how do we -- how is that decision made? I mean, for example, if this started right from beginning and the Guidant was the only one, that would have come straight into a 600 source.

DR. AYRES: I guess there's two factors to consider. One is, by virtue of these being beta sources, except for the Cordis, the rule making, we would have to create a whole new section for therapy beta sources, brachytherapy sources, beta emitters. Not a trivial operation. There's also, and this would be up to management to make a decision, but there's also a lot of talk and indications that this may be a -- this may have peaked and be on the decline because of drug-eluting stents.

When there's -- you know, it's being handled well, I think, and not an overdue burden on the staff licensing these under guidance at this point. And clearly, if it looked like a technology that was going to stay around for the next few years I think, you know, we should be looking ahead to rule-making at some point. But by the time we could do a rule-making on this, they may not be around anymore.

CHAIRMAN CERQUEIRA: Jeff.

DR. WILLIAMSON: Well, I think, you know, especially with some of these devices where it looks like there are design issues that really challenge the skills of the licensees, I would encourage you to keep track of the denominators in this business, because the --

DR. AYRES: Well, as you know, it's something we always have a hard time getting.

DR. WILLIAMSON: You have waxed and waned very quickly and so, you know, it's important, I think, to keep an eye on trends.

DR. AYRES: Yeah. I wish there was a good way to get those. And we've always done poorly. And this is something the Committee might be able to provide some valuable insight on.

CHAIRMAN CERQUEIRA: Well, I think the manufacturers could probably -- although I guess once they get them out to you, they don't trend them.

DR. BRINKER: It's roughly 50,000 a year. The restenosis, coronary restenosis, there are about a million angioplasties done a year now. Restenosis rate overall is about 20 percent. Now that's going to change drastically with the drug-eluting stents, so there's about 150,000 potential procedures that come -- that are potential brachytherapy procedures, and only somewhere around a third of them actually get brachytherapy. So

it's roughly 50 percent. My understanding is that the significant majority of them are the Novoste devices for a variety of reasons. And I don't -- I take one point with Jeff, and that is, I don't think that in the Novoste device it's -- a technical challenge for the physicians is turning the Touhey too tight. I don't consider that an unsurpassable challenge.

DR. WILLIAMSON: Well, it doesn't mean to say it's unsurpassable, but it is -- it takes a certain amount of care.

DR. AYRES: There's another large group of events that weren't directly addressed by the guidance. All of it relate to human factors issue with the Novoste device, and I'll go to my other advocation, if you will, as a flight instructor. I know the one thing a human can't do, and my students in particular, is hold a constant pressure. Your muscles just relax, and pretty soon what started out as say 5 pounds of pressure is a half a pound. And this device depends on that. There's an indicator but you've got to watch it, that you've got enough. And that's generally the cause of the source drips.

There's another type of incident. When these struck sources occur, and they do an emergency bail-out, part -- you shut the valve which locks the

sources in the safe, and then disconnect the catheter. It goes in a plastic box. Well, in doing this, it appears, because there are so many incidents, over 10, that probably released that plunger a round that time. That causes a fluid surge, and they dump sources all over the floor, and in the box. There's at least 10 instances where they spread the sources around the cath lab. Including one I thought was an interesting report, they identified one of them being on top of the survey meter knob.

DR. WILLIAMSON: I'll just rephrase my comment that, you know, this system is not as foolproof as the typical system we have for remote delivery in radiation oncology.

DR. AYRES: Exactly.

DR. WILLIAMSON: It takes a lot more care, and --

DR. AYRES: By order of magnitude.

DR. WILLIAMSON: These were stupid errors that caused these problems.

DR. AYRES: As somebody asked me, I'd estimate by an order of magnitude.

DR. WILLIAMSON: Yeah.

DR. NAG: When you investigate an event, have you found any correlation with the training and with

the *, to happen more through individual authorized user or individual person really for the first time, or second time, versus those who have done 100 of them?

DR. AYRES: Well, I'm sure that the Touhey, the burst valve or its equivalent issue is something that would diminish with experience, in general. But, you know, some of these things come along. I mentioned this crimping of the new three and a half. The most senior investigator in the field that I'm aware of just had two in a row.

DR. NAG: But that's a new catheter.

DR. AYRES: Well, I know, so I say experience doesn't apply to a change, but if you're accustomed to working with something for a long time, yeah, there's no hot spots. In other words, we're not seeing multiple of these events from the same licensee. They're just spread all around, and across broad-scopes, as well as limited-scope, and so forth. So I think it's an individual -- it's how -- there's no calibration on that. You have kind of like some devices that have a torque limiter on it, that don't allow you to tighten passed it. You start slipping but, no. Yeah.

CHAIRMAN CERQUEIRA: Ralph, I was just going to respond. Someone was asking about getting a denominator and how many times the sources were used, or

how many administrations occurred. I can't speak to the Protis unit, but I know that the Guidant, they record every time the dummies and the sources run out, and that's part of a computerized record for each device. That goes back to the manufacturer, so they probably have some statistics on that that might be able to be obtained.

DR. AYRES: Yeah.

CHAIRMAN CERQUEIRA: And Novoste, I think pretty much also keeps a pretty good track record of the number of patients that are done with their device from the various users. You might not get 100 percent, but I mean at least you'd be able to get --

DR. AYRES: I think the Novoste record too. It can only be read-out by the vendor. I know it shuts down after so many.

CHAIRMAN CERQUEIRA: Right.

DR. WILLIAMSON: They sell catheters that are specific to each patient.

DR. AYRES: Yeah. It's catheter sales. If you don't mess up the catheter, there's probably a few lost too.

DR. WILLIAMSON: I think these companies know probably fairly how many --

CHAIRMAN CERQUEIRA: Yeah, they could

provide that information.

DR. AYRES: Yeah, the same way with -- even though the Cordis system's traditional seeds and ribbon can be used an indefinite number of times, there's still -- I think it's keyed on the catheter sales, like you said. We just don't get those figures. I'm not even sure that we have the authority to go out and ask for them. And unless they want to voluntarily supply them, we're not going to have that information.

CHAIRMAN CERQUEIRA: Okay. All right. Any other questions for Bob? Thank you.

DR. AYRES: Okay.

CHAIRMAN CERQUEIRA: And we managed to get far enough behind to be on schedule again, so this is break time, so maybe we should take the 15 minute break. I notice a lot of nodding people around, and we'll get back at 3:15.

(Whereupon, the proceedings in the above-entitled matter went off the record at 3:01:25 p.m.)

CHAIRMAN CERQUEIRA: All right. The subcommittee working group and the stakeholders will be starting now, and Ruth is chair of the subcommittee.

Why don't you take over?

MS. McBURNEY: Okay. The Subcommittee on

the Emerging Technologies was set up to provide input and guidance, advice to the NRC staff on some of these emerging technologies, although our first charge is to review the licensing guidance for IVB Y-90 microspheres and GliaSite. I think it was -- correct me if I'm wrong -- is to be available, maybe doing some position papers on some of the even newer technologies as they come out to help NRC staff in developing licensing guidance for those as well.

But as far as what we'd like to do this afternoon is to get input. We were asked to get input from stakeholders and also among ourselves as to the appropriateness of the licensing guidance for these three modalities.

This morning, you know, we discussed some issues dealing with user training, acceptable user training for the microspheres, and as we go through these, the issues of physician training, whether there's to be a team approach, what that team should be comprised of, who should be present during the procedures, what the contents of the written directive should contain. I think there's been a lot of discussion on that as well, and any other radiation safety procedures that you all feel are important.

So I guess we can start with the

microspheres. There are several people in the audience that would like to provide input on these discussions. I know that ASTRO has a couple of people here and probably the Society of Nuclear Medicine as well.

So as those who want to comment could come up to the table so that we could have sort of a dialogue. I hate to look behind me all the time.

CHAIRMAN CERQUEIRA: Right. Maybe if one person from each of those groups could come up.

MS. McBURNEY: Right.

CHAIRMAN CERQUEIRA: We've got two chairs at the front. I guess we need one intravascular, one radiation oncologist and maybe one nuclear medicine.

DR. WILLIAMSON: We are talking about Yttrium 90 now or are we --

MS. McBURNEY: Yes.

DR. WILLIAMSON: -- going to talk about intravascular brachytherapy?

MS. McBURNEY: We're going to start with Yttrium 90, and then GliaSite and then IVB.

DR. NAG: Yttrium 90 would be from nuclear medicine and from ASTRO?

MS. McBURNEY: Yeah.

DR. WILLIAMSON: So can I ask a question, just a procedural question?

MS. McBURNEY: Yes.

DR. WILLIAMSON: You know, the licensing guidance for IVB has been reviewed several times within this group.

MS. McBURNEY: Right.

DR. WILLIAMSON: What exactly is our charge with respect to that?

MS. McBURNEY: Just to review it. If you think it's adequate, say so and we can just go on from there. Would you prefer to start with that and get that out of the way?

DR. WILLIAMSON: Oh, no, no, no. no.

CHAIRMAN CERQUEIRA: No.

DR. WILLIAMSON: I was just wondering. I understand with the other two, you know, they're very new, and there are substantive issues there. I was not aware there were substantive concerns.

MR. MARKLEY: I just wanted to mention if other people want to sit at the side tables, we have microphones here as well.

MS. McBURNEY: Okay.

CHAIRMAN CERQUEIRA: And there's always microphones at the back.

MS. McBURNEY: And for those other than the committee members, just identify yourselves as you speak

and we'll recognize you.

So as was discussed earlier, Yttrium 90 microspheres is considered a sealed source, but it's possible that it could be licensed to someone trained in radiopharmaceutical therapy. Some of the states are already doing that, and others require the training and experience for manual brachytherapy as a classification.

So if we could just start with the physician training issue for that, I think there has already been a lot of discussion on that, and that we had some concurrence that either of those, with appropriate vendor training, would qualify.

DR. EGGLI: Yeah, as a comment on that, I think that we wouldn't be looking at all of the 300 series users, but specifically the 390 users who have a bit more experience and training and probably have been doing therapeutic activities which are similar in complexity and scope to the microsphere injections.

And again, acknowledging that there probably should be an authorized user who participates, and that authorized user might be someone with both 300 series training or 400 series training, depending on the unique needs of the institution and what kind of teach approach those institutions use.

DR. NAG: I think it's very important to

harp less on the team approach because if it definitely goes to the wrong place and that's not being pushed by either the 300 people or the 400 people, you're going to have a problem.

So the team, your thrust with the team should have somebody who is doing the distribution study. If the distribution study is wrong, you're going to have a problem.

Someone, which means a nuclear medicine, include a nuclear medicine person for that.

The introduction of the catheter, whether it be done by a interventional radiologist or at the time of surgery by a surgeon, by someone who has knowledge of the tumors because if you don't have the knowledge of the tumors and how they respond and behave with radiation, you're going to have problems, and that would be either a radiation oncologist, surgical oncologist, or a medical oncologist.

And an installation of the radioactive material itself, which could be either the 300 -- someone with the 300 training or the 400 training.

So this should be a team approach rather than only one person doing it because if they make a mistake in any of the other portions, you're going to have a problem.

DR. EGGLI: I think one of the considerations, since this is called a brachytherapy device, is lost source recovery because I can tell you what. This lost source recovery isn't a 400 activity. It is a 300 activity because this is going to be like a spilled radiopharmaceutical as far as its recovery goes.

DR. WILLIAMSON: So that is a good question. Have you given thought to the threshold before there has to be a lost source reporting requirement?

DR. HOWE: No, we didn't. We assumed that the radiation safety officer would be able to handle it if they had a spill, and you would be trying to wipe up this stuff. It's a --

DR. WILLIAMSON: So you would use the same kind of criteria as for a radiopharmaceutical spill to determine it was all cleaned up.

DR. HOWE: And this would be one of the unique properties of it. It's teeny-tiny. So you're not going to be able to count it. You're not going to be able to see you got all of it back that way. You use a different alternative.

DR. EGGLI: Well, you'd be able to count it with a counter, a radiation counter.

DR. WILLIAMSON: Well, can i say something about the team approach? I mean, clearly team approach

is a good thing, and it should be used in medicine wherever it's indicated in multiple specialties, but you know, the only reason it got into this regulatory arena was because intravascular brachytherapy was ruled to be by the FDA to be a high risk procedure, and therefore, the NRC felt impelled and I think rightfully so to incorporate some of the FDA guidance that was part of the clinical trial protocols at that time, and so that's how it appeared in regulatory space.

So is it necessary to regulate to that level of detail here?

DR. HOWE: Let me just make a quick comment, and that is that some of our therapy ones are team approaches, and before the new Part 35 for the gamma knife, we had the neurosurgeon, the radiation oncologist, and we had the authorized medical physicist.

When we did Part 35, we decided we could not set the criteria for the neurosurgeon. So we dropped the neurosurgeon out of our regulations with an understanding that at a medical facility you're not going to drop a neurosurgeon out, but we couldn't define who was supposed to be the neurosurgeon.

So if we go for a team approach with these, then our guidance will probably only identify those team members that have radiation safety training, and then you

as a medical community can insure that you have the right other medical.

We did the same thing with intravascular brachytherapy. We don't address the cardiologist, although everybody recognizes that the cardiologist will be there because the true cardiologist is not a nuclear cardiologist. We don't have criteria for that. Everybody understands he's going to be there, but he's not in our requirements.

DR. AYRES: And another longstanding one like that that we've never regulated the other team member is the permanent implant, is the prostate, which often classically involves a urologist.

MS. McBURNEY: Ralph?

MR. LIETO: Yeah, along the same lines, I agree it should be a team approach, but I think we have to give, I think, guidance as to who can be specified there. You know, I think one team member is obviously the authorized user has to be there. I mean he should dictate really if he needs an interventional radiologist, I mean, whoever it is at his facility, whether it's an interventional radiologist or interventional cardiologist, whoever. Okay?

Let the authorized user determine who the other team members should be for the appropriate

delivery, and then, you know, obviously you're going to have to have someone to address the issues of emergencies, and if there is a spillage, are you going to have the authorized user responsible?

DR. AYRES: And dosimetry.

MR. LIETO: I don't know.

MS. McBURNEY: Jim.

DR. HEVEZI: Jim Hevezi, speaking on behalf of ASTRO.

I think ASTRO's position is also the team approach for many of these new technologies, and, you know, I think it has always been in our purview to include interventional cardiologist, radiation oncologist, authorized medical physicist for intravascular brachytherapy, for example.

Now, I know the rules are written a little differently, but at one of our institutions that I do this with we've always included all three, and they've always participated in that.

MS. McBURNEY: That's for the?

DR. HEVEZI: Intravascular brachytherapy.

MS. McBURNEY: Right.

DR. NAG: Now, we are dealing right now with --

DR. HEVEZI: I'm sorry. Even in this regard

with microspheres, I mean, I think the process of cure is an important consideration for ASTRO in this regard, and that is the patient could have had external beam therapy for these tumors before the yttrium microspheres are injected. We may have to access dosimetric consequences of additional radiation therapy to some of these sites.

In the liver, for example, I know up coming -- you don't have to deal with this -- but IMRT is used now in a stereotactic methodology to treat liver nodules, and so --

CHAIRMAN CERQUEIRA: But that's really practice of medicine in terms of --

DR. HEVEZI: I agree.

CHAIRMAN CERQUEIRA: -- who does it, and I think here -- and I guess, you know, the issue comes down to do you need a radiation oncologist there or can a nuclear medicine physician make some decisions about, you know, the dosimetry and all of the other decisions.

DR. HOWE: I think it would be more helpful if you talk in terms of what different tasks are as opposed to identifying an individual, and then once everybody figures out what the tasks are, then it will be much clearer from our part which part of those tasks go to our people and then --

DR. EGGLI: The training and experience

required for each one of those.

DR. HOWE: Right.

DR. NAG: Right. I mean, in that regard what you're bringing up is radiation tolerance of an organ. Now, unless you know how much radiation that organ has received before, you cannot know how much more that area can tolerate.

For example, if the upper abdominal radiation quadrant is or isn't, or for the same disease to other site, you need someone who will be able to analyze that before you determine (a) is this basically safe.

Now, someone can inject it, but before the injection, someone needs to make the determination, and the only --

DR. HOWE: And we're agreeing. We're just saying talking about it in tasks or --

DR. AYRES: An example of two tasks would be shunting them.

DR. HOWE: Right.

DR. AYRES: The task would be determining the dose that's going to be received by the amount shunted, and the medical decision on what to do or not to do about that. If it was a sufficient amount to cross the injury threshold to the lung or to the GI system and

what could be done and what should -- what kind of effort, and this is radiation expertise and decisions and medical decisions related to that.

Those are the kind of things.

DR. WILLIAMSON: What Subir is trying to get at is who can be the prescribing physician.

DR. HOWE: Right, but I think if we talk about it in terms of task first and figure out what all of the tasks are, then later on it will become clear maybe who that is or maybe there's multiple people it can be.

DR. WILLIAMSON: Then the first task, I guess, he has identified is patient selection, taking a history, and determining the prescription.

MS. McBURNEY: Doing the written directive.

DR. WILLIAMSON: This is before the written directive. So this is patient selection and formulation of treatment intent.

DR. HEVEZI: Yeah, I don't think ASTRO is opposed to having other, you know, specialties involved in this. Not at all. I think, again --

CHAIRMAN CERQUEIRA: I'm not chairing this session now. Ruth is.

MS. McBURNEY: Yeah.

CHAIRMAN CERQUEIRA: So I can --

MS. McBURNEY: So you can comment.

CHAIRMAN CERQUEIRA: Yes, I can certainly comment, but again, in looking at the nuclear medicine analogy, these guys treat thyroid disease. They're making those same types of decisions. Some of these people have had previous surgery. They've had, you know, radiation to other things as well, and certainly in terms of the decision making for the treatment I don't see any problem with having, you know -- I agree with you that that's a function, and I think what the staff is trying to do is get away from individuals and just look at the tasks so that we avoid the turf issues.

DR. HEVEZI: And I think that's a good way of dividing it.

CHAIRMAN CERQUEIRA: Right.

DR. EGGLI: So there are a series of tasks that have to be performed here. If you look at it, there's patient selection, and then there's an evaluation of the impact of the proposed treatment on the patient, which is some form of dosimetry.

The next task is more mechanical, which is essentially installing a delivery system. Then the next task is actually instilling the treatment dose, and then finally, after removal of the treatment devices, determining that the area has not been contaminated and

as best as possible, determining that the treatment dose was delivered to the intended volume and that there are methodologies for doing each of these tasks.

And I think a variety of people are able to do this. I think probably the dosimetry part, at least the biodistribution part is likely to be at this point, unless -- at this point is likely to be a nuclear medicine type procedure, or it could be a few years ago there were iodinated microspheres for the liver that were nonradioactive and could be done with CT. I don't believe those are FDA approved or readily available currently, but you have to have some way of evaluating the volume of distribution of the treatment, and you have to have some way of figuring out the collateral damage.

And likely that's going to be an unsealed source radiopharmaceutical that will be used to make that determination as one of the various steps, and again, one of the keys of the success of this procedure is going to be making sure that the conditions of the dosimetry are precisely reproduced for the therapy, and one of the key items there, again, is infusion rate.

If I change the infusion rate between my dosimetry study and my therapeutic study, the biodistribution of that material is going to be significantly altered. And I've seen this many times

with liver therapies which we're currently doing, and by testing that hypothesis, by changing the infusion rate and looking at the biodistribution of, as a matter of fact, the particulate radiopharmaceutical that we're using to determine the biodistribution for chemotherapy purposes.

I can dramatically change that biodistribution by changing the infusion rate. So I think a key item in this whole process is that the conditions of the dosimetry must be precisely reproduced for the therapy, and so that at some point the person involved in the dosimetry is going to have to participate in the therapy, in part, to try to insure that the conditions of the dosimetry are reproduced for the therapy or at least there has to be some very clear communication about the conditions of the two events.

DR. HOWE: And I kind of see isodose curves and normal things that a brachytherapy medical physicist would do and an oncology brachytherapy physician might do as being equally as relevant. So maybe someone on that side can talk about it.

MS. McBURNEY: Ralph, Jeff or Jim?

DR. HEVEZI: One thing we do a lot in some of our other brachytherapies is do a pre-plan, and you know, perhaps the test dose that we speak of, a pre-plan

could be run on that to see, you know, what if you use the total therapy dose, what those distributions would look like.

DR. EGGLI: How fast can you do a pre-plan?

DR. HEVEZI: Right.

DR. EGGLI: I mean, this needs to be done immediately --

DR. HEVEZI: Well, real fast.

DR. EGGLI: -- in continuity, like minutes before the actual dose is infused because you will not reproduce the conditions of the infusion on another occasion.

DR. WILLIAMSON: My impression is they don't do isodose planning for this typically, but you do some kind of an average volume, average dose in a volume kind of calculation based on quick analysis of the --

DR. EGGLI: And probably a MIRD type equation.

DR. WILLIAMSON: Yes, exactly.

MS. McBURNEY: Dr. Diamond, did you have your hand up? I can't see you down there?

DR. DIAMOND: Oh, yes. That's my problem.

Donna-Beth, I think the way you're approaching this is very useful, and what Doug said was very helpful to my thinking. So let's think through the

steps.

Patient selection, dosimetry, actually patient selection, delivery system insertion, dosimetry, administration of therapeutic dose, and assessment both for biodistribution, for efficacy, and for possible contamination.

Those are the steps. Let's work through them.

DR. AYRES: I would just mention that insertion is a critical one that can influence the distribution, too. You're aware of that.

DR. DIAMOND: I'm aware of that, yes, sir.

As far as the delivery system insertion, meaning the actual placement of the catheter, all right, well, that will be done by interventional radiologists or perhaps a surgeon, whether it be a general surgeon or a specialist in abdominal or hepatic surgery, and I think we're all clear on that.

And it's really not germane to discuss that any further. It's outside of our purview.

As far as the dosimetry per se in a real time basis, my sense is that the nuclear medicine folks are better at that than we in radiation oncology.

I would also state that as far as assessment of the biodistribution, they probably are better at that

due to their training than we are.

I think that with respect to the actual administration, the actual physical installation of the therapeutic dose, I think it is inconsequential whether that authorized user is either a radiation oncologist or someone with 390 type training, provided they have certain specific -- a certain degree of similarities in training and experience.

In other words, not every single 390 user, I think, would fit.

And then finally, one of the most important steps as far as patient selection, that is probably the step that I think the radiation oncologist would be by far the best suited for because if you think about this, right now we're looking at therapy only for hepatocellular carcinoma. However, it is certainly conceivable that this type of modality in the future will be used in the treatment of metastatic disease to the liver.

And where do these arise from? Colorectal, breast, pancreas, and so forth, and therefore, essentially by definition, many of these patients will be extremely highly pretreated, whether it be from medical oncology and/or from a radiation oncology standpoint. And I think it is general oncologic knowledge that really

we may provide the most value in.

So when I approach all of the steps that Doug outlines, I think that the delivery system insertion is taken care of and is outside of our purview. I think the assessment of the biodistribution both for efficacy and for possible contamination or complications really falls into the nuclear medicine sphere.

I think it is inconsequential really physically who is instilling the therapeutic dose, whether it is a radiation oncologist or a nuclear medicine specialist in 390 with special caveats, but I really think that the patient selection issue, particularly since it's highly conceivable in the next year or two that this will fall into a much wider range of patients, many of whom will have been heavily pretreated with radiotherapy and with chemotherapy, and that's really where our chief value may be.

This is a personal opinion.

DR. NAG: I'd like to correct you on one thing. There's a difference between TheraSphere and SIRSphere. TheraSphere is now called cholangiocarcinoma. The SIRSphere is now approved only for metastatic tumors and not for cholangiocarcinoma.

DR. DIAMOND: I'm sorry. TheraSpheres --

DR. HOWE: One has to understand the

practice of medicine will expand the use of theraspheres at this point.

DR. NAG: Yes, right. But I'm saying even at this point SIRSphere is only for metastatic tumor, and TheraSphere is for cholangiocarcinoma.

DR. DIAMOND: Firstly, I was only speaking about Therasphere for this particular point, and it's actually not for cholangiocarcinoma. This is for hepatocellular carcinoma.

DR. NAG: Right. I'm sorry, yeah.

MS. McBURNEY: Ralph.

MR. LIETO: Just not having been involved with microspheres, I just wanted to get a point of clarification, and I think it might involve a task that's been missed.

The administration of the radioactivity, is it based on volume or is it based on a dosage, in other words, an amount of radioactivity? Is there a prescribed radioactivity, a prescribed volume or some other means that determines what is delivered?

DR. HOWE: I think what's happening now is you're ending up with doses being delivered to specific lobes based on other considerations because these cancer treatment patients have gone through a lot of regimens. So they're --

MR. LIETO: Let me rephrase this.

DR. HOWE: Not necessarily millicuries. I think I'm really hearing --

DR. WILLIAMSON: You know, I think it's important to be clear of what is what. I get really confused.

DR. AYRES: The vendors have done the volumetric calibration that you've talked about, the dosimetry, and they basically said X millicuries equals so many grays in the tumor volume, and os it can be written either way, but if the intent is to deliver a specific amount of activity, slash, dose.

DR. EGGLI: But that's a huge assumption based on biodistribution, and if you have a nonuniform biodistribution, that is way off. This is basically using a MIRD assumption of uniform tracer distribution, and in fact, in these tumors that's very highly unlikely to be the case.

DR. AYRES: Well, in practice, that's an assumption. In practice, the intent is to deliver X millicuries. The misadministration would be determined on what percentage of that was successfully delivered or went the wrong places or what.

They're really measuring. The measured value is millicuries.

MS. McBURNEY: Ralph.

DR. WILLIAMSON: Can I ask a question of clarification?

MS. McBURNEY: Sure.

DR. WILLIAMSON: I'm a little confused just about the order of these things. So after patient selection, I assume a biodistribution study is done to determine how much --

DR. EGGLI: No. A catheter will have to be placed first.

DR. WILLIAMSON: A catheter is placed, and then a biodistribution study.

DR. EGGLI: Yes.

DR. WILLIAMSON: Then if there is going to be true dose point, then you know you have to do some calculations and select the activity.

Now, I'm going to use the word "activity" for activity and the word "dose" for absorbed dose, and so we don't get confused, I suggest that convention here.

Then the activity is selected and instilled, and where does the shunt business come and how does that figure into this process?

DR. EGGLI: Well, hopefully in the biodistribution study you will be able to assess the magnitude of the shunting. Again, these particles are

actually quite small, ten to 20 microns in diameter.

If you take a 20 micro particle, with liver shunting to the lung, ten percent of that particle will actually pass the lung and go into the systemic circulation. When you drop to a ten micron particle, the part that goes systemic is even larger.

And then you have to look at catheter replacement, and catheter replacement is key because if the tip is up against the wall, you get back pressure. It refluxes into the gastroduodenal artery. You get a big distribution to the gastric mucosa.

You're going to have to look at all of those things and you're going to do your best to make sure that the conditions of the dosimetry are reproduced.

Now, with the Y-90, we have an additional tool that we may be able to actually utilize to evaluate post treatment biodistribution, which is to do Bremsstrahlung imaging.

DR. WILLIAMSON: But to begin with, this biodistribution is done with a physically identical sphere that's tagged with a gamma emitter?

PARTICIPANTS: No.

DR. WILLIAMSON: No?

DR. EGGLI: The biodistribution will be done with a particulate material unfortunately slightly larger

in diameter with a wide spectrum of approximately ten to 90 microns.

So the spectrum of distribution will be there, but there will be some larger part.

DR. HOWE: I'm looking at the sealed source and device registry for SIRSpheres, and their product is supposed to be 32 microns plus or minus 2.5, and I think even TheraSpheres, because they can select out the size of these microspheres before they ever make them radioactive, and so they tend not to be at that --

DR. EGGLI: Okay. One of the documents in our binder says the diameter is ten to 20 microns.

MS. SCHWARZ: Can I ask a question? What actual pharmaceutical is being injected to do the distribution?

DR. EGGLI: Macro aggregated albumen typically.

DR. NAG: At least I'm not so sure about the TheraSphere, but on the SIRSphere they do the biodistribution study a couple of days in advance, and they order the number of millicuries based on how many are shunting into the liver -- I mean into the lung, and if the shunting is more than, you know, 30 percent, that basically is excluded.

DR. EGGLI: The problem with that is the

likelihood that you will reproduce the dosimetry conditions at the time of treatment is best described as remote.

DR. NAG: But that's how they're doing it. That's how it is being done.

DR. EGGLI: You know, that's a real risky proposition

MS. McBURNEY: Dr. Brinker.

DR. BRINKER: Can I ask whether the delivery system, being sort of a plumber here, the delivery system is prescribed by the vendor or can you use any kind of catheter?

DR. NAG: Any kind.

DR. BRINKER: Then why not use a balloon occlusion catheter and that way there will be no reflux?

DR. EGGLI: Even with a balloon occlusion catheter --

DR. BRINKER: I mean, there's got to be minimal, if any.

DR. EGGLI: More than you would expect. I mean on the current liver therapies we're doing we use a balloon occlusion. We get a lot of reflux into the stomach.

DR. HOWE: My understanding is they're in some cases using the balloon occlusion, one, to help

insure it goes more into the liver to avoid some of the shunting, but the delivery system itself in our terms, it is that box that you use to get the microspheres up into solution and then the catheter.

MS. McBURNEY: Yes, sir.

DR. WHITE: Jerry White, American College of Radiology.

I guess two questions really, nothing to contribute at the moment, but the question about the prescription that you raised, whether it's going to be activity or absorbed dose, I think it's still unclear to me. I want to assume that how you mentioned activity, the NRC is not taking a position that the written directive must be in terms of activity.

If a physician decides he or she wants to prescribe absorbed dose, is that acceptable?

MS. McBURNEY: I think that will be one of the things that we'll discuss.

DR. WHITE: That would be an important thing to at least have on the record.

DR. AYRES: The issue that Dr. Nag brought up, and there's a good physical reason for that in the separation between the imaging and the administration, is you can't subdivide a dose because it's not a homogeneous mixture that you can take an aliquot out.

So you have to tailor. You have to determine what dose you're going to deliver and then order it in that manner.

MS. SCHWARZ: I had another question on the actual delivery and receipt of the radiopharmaceutical.

So once you've determined by the biodistribution the actual dose that you will be injecting, if you are not drawing it up in house, you have to order it. So you have a patient lying with the infusion set, waiting for a dose to come? How does that happen? I just don't know. Is it a unit dose that's coming in from a centralized pharmacy?

DR. EGGLI: We have a central pharmacy 15 minutes away from us.

MS. SCHWARZ: I mean, so most sites would then be -- unless you had someone in house that's going to do that for you?

DR. HOWE: And it's not a radiopharmaceutical.

MS. SCHWARZ: Excuse me, but that's my background.

DR. AYRES: It's a device. The transfers come in a patient dose.

MS. SCHWARZ: Right, okay.

DR. EGGLI: But the issue on this suspension

is once you get it into suspension, you can administer a portion or all of the dose, once you have it suspended.

DR. HOWE: I think originally there was the concept that you would order the activity, and you would deliver all of it. What we're seeing with the SIRSpheres is that there is a medical endpoint that may be nowhere near putting all of it in because we're beginning to recognize you fill the slots.

DR. EGGLI: And I think that that's a reasonable approach.

DR. HOWE: Yes.

DR. EGGLI: A very reasonable approach because, again, if you can suspend it, you can deliver a fraction of it.

The other thing that we're very comfortable with is, you know, we lose parts of our dose all the time, in both diagnosis and therapy, and once you have experience with the process and your delivery device, generally you have a reasonable idea of the portion you're going to lose in the delivery device and you compensate for that typical loss.

DR. HOWE: But the loss we're seeing with the dose are generally due to poor engineering.

DR. EGGLI: Yeah, and once that's solved, there may not be an issue. Again, once you have it in

suspension, and you can suspend; we do it all the time. You can suspend 40 micron particles in a fairly uniform suspension.

DR. AYRES: That doesn't work with the glass ones. The SIRSpheres are much more successful. The TheraSpheres settle out very rapidly. The SIRSpheres settle out, but not nearly as rapidly.

DR. AYRES: Maybe one of the engineering things is to create a delivery device that continues to agitate the vial so that it stays in solution.

DR. HOWE: That's what they do, and they wash through continually agitating, but I think what we're beginning to see, based on what the experience is with the SIRSpheres with the imaging and maybe TheraSpheres will go in that direction, too, is more imaging as you go along to make sure that once they filled up the capillary bed, they don't keep pumping these spheres in.

DR. AYRES: What the two systems depend on essentially, the spheres, is fluid turbulence, and it's not a very efficient or very, in my opinion, particularly good design.

MS. McBURNEY: I think there were some hands up there.

DR. TRIPURANENI: Prabhakar Tripuraneni for

ASTRO.

And I think I enjoyed the eloquence of both Dr. Eggli and Diamond walking me through the various steps that are involved and the various people that are involved, and I think I support that on behalf of ASTRO.

DR. WHITE: Just with the listing of the various steps it might be helpful if we went through the steps now and looked at which of those steps were of interest to the NRC, that is, which were amenable to licensing decisions by the NRC because it's not clear to me.

Are all of them? I suspect they are not all --

MS. McBURNEY: Are you interested in all of the steps or those that just directly relate to the administration of the --

DR. HOWE: I think the decision points, and they may be based on information gathered from other folks, are going to be beyond the range of the oncologists and the oncologist is going to be inputting information to come up with a dose based on other treatments. For this individual patient there's not going to be any such thing as a unit dose like you've got or other procedures, like you get four millicuries of Strontium 89 for bone palliation.

It's going to be a patient by patient treatment is what we're seeing now. So that input will need to get into whether that's the authorized user or there's another authorized user. That information has to get into the authorized user in order for the authorized user to do the written directive.

So that's how that fits in.

DR. WILLIAMSON: Well, I think historically the interest of NRC has been relatively limited in this because that's the practice of medicine.

MS. McBURNEY: Right.

DR. WILLIAMSON: You know, as I mentioned earlier, with the high risk percentages --

DR. HOWE: We don't care about the number, but at some point the ultimate user has to do a written directive.

DR. WILLIAMSON: Right. I mean, the extent of interest is basically to, you know, limit the regulation to a personage who has some clinical experience, and then whatever decision they make about mixing TheraSpheres with some previous treatment is beyond the scope of regulation so long as the authorized user has the appropriate clinical credentials.

PARTICIPANTS: Right.

DR. WILLIAMSON: So there is a connection

between clinical competence and licensing at that point.

DR. AYRES: Right, which is why we retained the clinical component in the training and experience for the higher risk therapies.

MS. McBURNEY: Yes, sir.

MR. UFFELMAN: I just wanted to comment. Bill Uffelman for the Society for Nuclear Medicine.

You mentioned Zevlin earlier, and it's interesting because we just went through the process with the AMA and the ROC, and the process of care, which is much like what Dr. Diamond mentioned, but in fact, in Zevlin therapy, you know, there's a referral of the patient to either a radiation oncologist or a nuclear medicine physician who, in fact, evaluates the patient's prior treatments and record and all of that, and in fact, based on a whole lot of input may, in fact, involve medical physicists in literally evaluating what kind of organ dose has this patient previously had, and then makes a decision that they will then do the evaluation study in week one with indium and then move on to the yttrium if they pass that study.

But that decision process of referring the patient for the therapy process, in fact, is a medical decision made by a physician who knows what they're doing.

DR. DIAMOND: All right. So to help you out, Don, about the -- Robert -- we need to be a little more specific. The regulations will only -- only are germane to that issue regarding the authorized user training and experience, period.

Within the guidance we can go and give some additional sense of the NRC, and I think that's how we'll have to proceed. What I would suggest, therefore, is that in the text of the guidance that we go and convey this sense of the team approach, enumerating just for illustrative purposes the various steps involved.

And I would feel comfortable within that guidance also indicating that both the radiation oncologist and the nuclear medicine specialist qualified for 390 uses who has particular experience in these modalities would be eligible to be the authorized user, and, therefore, you actually have a body of guidance trying to convey to the stakeholders how we would like to see this develop.

It's not statutory, but it is within guidance, if you will, and we have referenced specific areas of the regs. which is, I think, what you need for your particular position.

Is that a way to move forward on this?

DR. HOWE: I think so, but one thing I don't

feel comfortable yet with the 390 because I think the 390 is a special kind of 390. I don't think it --

DR. DIAMOND: That's exactly what I'm saying. What I'm trying to convey to you is it's not just 390. It's 390-plus.

DR. HOWE: And so we need to identify those areas that are in the plus because it's not a 390 physician that gives four millicuries --

DR. DIAMOND: For example, earlier today Manny was asked a hypothetical. Would you feel comfortable giving, you know, I-131? And he said, "Of course, no. I haven't thought about that in 50 years, 60 years, 70 years.

(Laughter.)

DR. DIAMOND: So again, that is some practice in medicine, but I think we need to be in this particular instance a little more definitive. We don't want people to get hurt. If we've learned any lesson from vascular brachytherapy it is that by being a little perhaps too proscriptive to start and then loosening up with off-label uses, it probably was a really smart way to proceed.

So I would be in favor of a 390 plus or radiation oncology --

DR. WILLIAMSON: Here's another suggestion.

It's right now if you allow 300 users as authorized users --

DR. EGGLI: But not all 300 users.

DR. WILLIAMSON: Yeah. Let me finish my sentence.

DR. EGGLI: Three-nineties are already a subset of 300 users.

DR. WILLIAMSON: Yes. Well, right now, you know, the way the regulation is written, it defaults to Subpart J, which would allow the 80 hour people to get in. So I think explicitly making sure that it's limited to those that meet the full 700 hour requirement and have the full, you know -- are able to be authorized user for the full spectrum of radiopharmaceuticals as intended by the original new regulation would be one place to start, and another way to maybe get the plus is the time honored method of having a supervised case experience prior to being allowed to be an independent authorized user, that you have to be supervised by an experienced, authorized user for the first one or two cases.

Something like that might be the way to get the plus in there.

DR. EGGLI: Are you going to separate broad scope licensees from limited licensees in that?

DR. WILLIAMSON: I think that this guidance

is explicitly aimed at limited scope licensees.

DR. HOWE: And I think part of that is that we assume a broad scope licensee is a whole spectrum of other people that can help out and bring everybody up to a speed that the limited specific isn't going to have that back-up or safety net.

DR. AYRES: This is exactly the place where we're looking for advice from the committee. If you propose something like 390 plus, what's the plus and what's appropriate?

DR. WILLIAMSON: A supervised case experience.

MS. McBURNEY: And specific --

DR. WILLIAMSON: That's the logical way to do it.

MS. McBURNEY: And specific vendor training?

DR. WILLIAMSON: Yes, and specific vendor training.

DR. AYRES: That's the sort of thing that advice -- because that is the sort of thing you put in the guidance for conditioning.

MS. McBURNEY: That's what I would think is the specific vendor training plus case preceptor --

DR. EGGLI: You can ask the community. The regulated community can ask the vendor to create

opportunities for the plus if it's determined that there has to be a plus on the 390.

You know, in a crass commercial sense, it's in the vendor's financial interest to, in fact, make available training opportunities so that the material can become widely available if it's appropriate that it should be widely available

So that if I had a limited license and I wanted to do TheraSphere therapy and there were a plus, I would personally go back to the vendor and say, "What are you doing? What's your program to get me there?"

DR. AYRES: But I think we'd like the impartial advice from our committee rather than the potentially biased --

DR. EGGLI: Well, no, but you determined the plus.

DR. AYRES: Yeah.

DR. EGGLI: I think that as a person who wanted to then become certified, I would go back to the vendor and say, "This is what the plus is. What are you going to do to get me to that point so I can get certified for this?"

I would personally go back to the vendor and discuss them, but to create a plus we need to create -- we need to make sure there is an opportunity for people

to get to that point because, again, otherwise we come back to what we talked about this morning, where there are hospitals that may not have the training expertise available to train the person who's going to become the authorized user.

So in thinking about this, there has to be a reasonable mechanism for end users to achieve whatever that plus is determined to be.

DR. AYRES: And Dr. Diamond brought up something else that gave me an idea, and I don't know whether Tom would agree with or not, but he was suggesting, basically what it sounded like to me, was suggesting putting some cautions and advice into the guidance, which we normally don't do because it's kind of short and sweet. This way you license the material.

But a new idea with the expertise in this committee might be get the committee involved in some of these new modalities in writing, what we call information notice, the cautions, what things you should be aware. You've got a lot of expertise to bring to the table that staff wouldn't have.

DR. DIAMOND: To me this is the best way of us being able to go and help the medical community without overstepping our bounds as to what is within our purview to regulate.

DR. AYRES: Well, an information notice is nonregulatory in any sense.

DR. DIAMOND: Right, exactly.

DR. AYRES: And it's supposed to be an expert view or expert advice on how to stay out of trouble in some cases, and it looks like the committee could be really valuable in some of them.

The original bulletin that we put out after the Pennsylvania death or the death in Pennsylvania heavily involved ACMUI and heavily involved radiation oncologists at the time. He contributed hugely to that. It worked out well.

DR. EGGLI: If I might, could I ask for both ACR and Society of Nuclear Medicine to make a comment about a 390 plus comment and how they would perceive that issue?

MR. UFFELMAN: As a former regulator I was going to suggest how many I'll call them supervised administrations, and I don't know if that's a proper term, but how many supervised administrations do you feel makes one a qualified. You know, is it two? Is it three? You know.

DR. NAG: I think the problem is going to be that there's not enough number of people who have employed this to be able to supervise the 50 requests for

licensee. So, you know, how are you going to get supervision and who are you going to supervise?

DR. EGGLI: I think the initial supervisors will end up being broad scope licensees who can create the kind of appropriate scenarios for gaining the experience because if nobody has experience, who trains?

And with the new things, at some point nobody has experience or at least very few people have experience. The broad licensees become the pool of people who will become the trainers. They have the programs that will permit them to get going on these things, and then you provide opportunities.

I guess the question is how common will the use of -- hepatocellular carcinoma is not the most common tumor we see every day of the week. The question is how commonly will something like TheraSpheres be used if they are not extended beyond the initial FDA approval for hepatocellular carcinoma. This may become a moot point because TheraSpheres won't be economically viable if it takes ten years to get enough experience for it to become widely used in the community. This product will die long before that.

So that unless this expands to indications beyond the treatment of hepatocellular carcinoma, it's probably not going to go anywhere anyway.

DR. HOWE: You have to consider SIRSpheres because SIRSpheres is out there for a broader and it's got a PMA and now can go into practice of medicine. There's probably an assumption that TheraSpheres will be coming behind it, and I'd like to talk about it more in terms of generic microspheres.

DR. EGGLI: The issue of that kind of product.

DR. HOWE: Yes.

MS. McBURNEY: Yeah, I think that any guidance we have we need to think beyond just how it applies to this particular modality, but also how it could apply to any other new modality. Do you want one or two case loads on those as well?

DR. WILLIAMSON: So how about just two cases?

DR. EGGLI: How does ACR see the concept of 390 plus?

DR. WHITE: Well, I'm going to ask Lynne Fairobent to say something about that, but before we do, one question is as we talk about what the plus is, it's still not clear to me we know what tasks the plus is designed to provide training and experience for, and we have this set of task lists. I'm not sure we've come to a consensus on which of those tasks will be --

MS. McBURNEY: Well, in my mind it has to do with using Yttrium 90, using a pure beta, trying to figure out what you've delivered radiation-wise, and I'm just thinking in radiation terms, and dosimetries in my mind are very important.

DR. WILLIAMSON: Would it be patient selection, writing the written directive, being responsible for all of the --

DR. EGGLI: No, because that's not an NRC regulatable activity.

DR. WHITE: We haven't decided yet I think is my point.

MS. McBURNEY: If those things are under AU.

DR. WHITE: Let's go through the list.

MS. McBURNEY: That the AU would do.

DR. WHITE: So it's patient selection and history?

DR. DIAMOND: I'm sorry. I got a little lost here.

DR. EGGLI: Which activities are NRC regulatable and which survive.

DR. DIAMOND: Right. That's very clear. NRC regulated activities simply relate to authorized user.

MS. McBURNEY: Right.

DR. DIAMOND: Period.

DR. AYRES: Yeah. Our input into that is the qualifications of the authorized user. That's where it ends.

DR. WHITE: But in the field I can't tell you how much time and agony we spend over what it is the authorized user can do. This is a source of great angst, and I've asked the question at the list. Patient selection history, yes or no, and I have both answers on the table.

DR. WILLIAMSON: Well, that's because it's not the business of NRC to dictate that.

MS. McBURNEY: That's right.

DR. WILLIAMSON: The NRC assumed that the AU is responsible for all aspects of writing the written directive and supervising the safety aspects of the treatment, period, end of story. They're responsible for the regulatory compliance with regard to that treatment.

DR. HOWE: And I'm assuming the AU knows enough about how to figure out what does is needed of a Yttrium 90 to treat this particular patient, and I don't know how he gets there, but that's what I'm assuming he has to know to write the written directive.

DR. WILLIAMSON: The NRC regulations aren't meant to resolve turf issues of who does what.

DR. DIAMOND: Except in a very --

DR. WILLIAMSON: -- patient were sort of zero with degree approximation, you know, at the --

DR. DIAMOND: But you see, what we're trying to do is in a sensible way accomplish both goals in one fell swoop by trying to use the guidance space to help provide the stakeholders some sense of how to proceed because if we don't do it, it's going to be a mess.

I mean that's the bottom line. We cannot make it statutory, but we can certainly put it in --

DR. WILLIAMSON: Well, you're asking maybe the wrong group to do it, David. I think to come up with a consensus process of how to do it, unless there are really extraordinary implications for patient safety, NRC is just not equipped to handle that. That's a task better handled by the medical society, I think.

DR. HOWE: And we probably can't resolve it here and today.

MS. McBURNEY: Right.

DR. HOWE: But we've got the bullets.

DR. DIAMOND: I don't know. Doug and I sense an agreement on at least the TheraSpheres. Prabhakar seems to agree, and Bruce seemed to be smiling.

DR. WILLIAMSON: I'm agreeing with your point. I'm simply reminding you that this is a federal

regulatory agency that has very limited focus what it regulates, and it's not in a good position to sort of dictate consensus guidance for clinically how a disease is to be treated.

DR. AYRES: Getting back to something that we do, I just want to bring this in. You mentioned a certain number of cases, training. Well, it's common practice in these new modalities. The vendor actually supervises these cases, and the vendor trainer is often not a physician.

And is that appropriate or is that what you'd recommend? What's the minimum requirements for the proctoring, if you would, or training for these things?

DR. EGGLI: Historically NRC has set thresholds for training for therapy experiences, and probably the thresholds should be similar to thresholds for other similar therapeutic procedures.

You know, in a lot of the radio pharmaceutical areas, the threshold is three.

DR. AYRES: But I'm saying normally we say often the classic is vendor training. Is that vendor training adequate? This is something the advisory committee --

DR. BRINKER: Well, what he's saying is you need a physician to come and supervise you or get a

trained vendor representative.

DR. EGGLI: I think if your issues are radiation safety, then I'll toss the ball back. The NRC should be able to determine what the criteria are to be a trainer for radiation safety. It may be that a vendor trainer may be sufficient.

DR. AYRES: In the IVB area we've had a number of medical events with the trainer right there.

DR. HOWE: And I'm not sure that we have an equivalent experience out there.

DR. EGGLI: Maybe you can rank order them in some way to say, "Okay. This experience is higher risk than this experience, whatever this is, but this is lower risk than this experience. What are the bounding parameters?" and select something within that boundary.

DR. HOWE: Like I'm not sure I'd consider somebody with a lot of experience in I-131 therapy to be in the same ball park with --

DR. EGGLI: No, but what we're talking about is a risk. You're saying, okay, I-131 therapies have this kind of risk. High dose brachytherapies have this kind of risk. If those are the kinds that you're determining are bound, let's just ask an example. That's not to say --

DR. HOWE: And I think the yttrium

microsphere has a very high risk.

DR. EGGLI: Okay. if they are bounding parameters, then you select something within that boundary that you consider representative of the risk. I'm not sure that they have quite as high a risk as you think they do.

There is the issue of the collateral damage.

DR. HOWE: And that's why I'm thinking they have a higher risk.

DR. EGGLI: But I do collateral damage assessment all the time. I don't know. Maybe not every nuclear medicine physician does. I can't speak to that, but the process of assessing the risk for collateral damage is really very straightforward.

It requires some accuracy, some precision, but the process of doing risk assessment is quite quantifiable. Give me 15 minutes and I can outline the procedure for you for assessing a technical procedure for assessing that risk so that the process of risk assessment is really quite a straightforward kind of thing.

So that the question again is where does your consider ride. If I can define a simple and straightforward procedure for assessing, where do you want to fall down on this question? Because I can define

a very straightforward process for assessing risk, and in fact, that's going to have to be done in any case.

DR. NAG: But then your problem, you have to define the risk of the procedure. Plus you have knowledge of what the followings is of the whole organ, the partial organ, based on how much pre-treatment there has been and how much pre-treatment there has been with chemotherapy, how much pre-treatment there has been with radiotherapy.

DR. EGGLI: But that's not part of the process that we're talking about here.

DR. HOWE: But a part is determining what --

DR. NAG: But it is.

DR. HOWE: -- the dose that should be delivered should be.

DR. NAG: Yes.

DR. HOWE: And making sure that that authorized user knows how to determine that when surrounded by all of those factors because this isn't a cookie cutter.

DR. EGGLI: Right, but this isn't secret information. There are medical records that in fact accurately record all that information. Now you have to say that someone has to integrate that information.

And there are proposals that suggest who may

be the best experienced to integrate that information, and that is part of the treatment planning process.

But if you want to look at the mechanics of the process of assessing risk to make the measurements that are used in dosimetry to make the determinations of what kind of dose a focal area of the liver is going to get, what kind of organ damage in a focal, versus global area, you are prepared to tolerate.

And those are fairly straightforward processes.

DR. HOWE: And I think you used a word that I think is very important here, is that this particular type of thing does use treatment planning.

DR. EGGLI: But treatment planning doesn't have a rigid definition.

DR. HOWE: No, it doesn't, but it is critical for this.

DR. EGGLI: And I think that treatment planning is an important part of the process in any radiopharmaceutical, because when I give someone 7000 millicuries of radioactive iodine, if I have not done the right type of treatment planning, I have killed their bone marrow.

And in 90 days, they are dead, and so treatment planning is part of any therapeutic procedure,

the treatment planning becomes more complicated as the risk increases.

But the process of treatment planning can be reasonably defined, and David and I, I think, are inclined to agree on what makes a good process here. I am not sure the NRC is comfortable in regulating in all of those areas where David and I might agree a process is reasonable. But the processes are quite definable.

DR. HOWE: And I think what I would probably be looking for would be those radiation points in that treatment planning to ensure that the authorized user has experience and training in those --

DR. WILLIAMSON: Could I make my parting shot before I leave? I think that we are kind of getting off on tangents here. Now, we had a consensus that a 390 qualification was a reasonable baseline, and there was some concern because of --

DR. HOWE: It is what is the plus.

DR. WILLIAMSON: Let me finish. I was not through. That 390 was a reasonable baseline, but because this is higher risk to the patient than many nuclear medicine pharmaceutical treatments, there is a desire to have or to assure some additional measure of clinical training.

So I think that suggests that you want a very simple to administer requirement that would bring the candidate authorized user in contact with the person who has the clinical experience so that you have set up the opportunity for that information to be transmitted.

So I would go back to the supervised case study concept as being the realistic and easily administered or easy requirement to administer, which would have a high probability of success in bringing these two people together and creating the environment for this information transfer, experience transfer, can occur.

And I think that is probably about the best that could be done. And I think to sort of try to micromanage it more and get in the position of being like ASTRO or ARC in writing standards of clinical practice, as well intended as David's suggestion was, and I think that the NRC is the wrong organization for that.

DR. DIAMOND: I would disagree a little bit, Chuck. I think that if we are creative outside of the statutes themselves, there is some space in informational documents that are not this binding by statute that we can go and convey a sense to the stakeholders what our sense of this is.

Because I recognize that if we don't provide

some context that it is going to be a mess. So I have no dispute regarding the letter of the law and the actual purview of the NRC from a trajectory point of view.

I also feel that there is some wriggle room in informational statements and so forth that I think would be very helpful.

DR. EGGLI: And there is going to be cross-education between 300 and 400 people, because 400 people are going to have to learn a little bit about dosimetry. a la nuclear medicine.

So there is going to be cross-training across 300 and 400 for these procedures.

MS. MCBURNEY: I would suggest just so we can move along to some of these other issues --Lynn, do you want to --

MS. FAIROBENT: Yes. I am Lynn Fairobent, Director of Federal Programs for the American College of Radiology, and after sitting and listening to all of this discussion, I think what is really perhaps not necessarily totally in NRC's purview, which is to ascertain what the additional clinical experience or training is needed over and above the basic 700 hours in 390.

My recommendation would be that ACR and SNM go back collectively in our nuclear -- through ACR

through our nuclear medicine commission, and SNM at large, and come back to the NRC from the clinician's standpoint what perhaps the additional, or what is the appropriate additional training that might be necessary, whether it is two cases, three cases, I do think that there is an adequate basis in the regulation for that additional training.

But I have also not been convinced by the NRC as to why there really is the need for additional cross-training under 390. And I have to agree with Dr. Eggli's last point.

I think that there is some circumstances for radiation oncologist trained under 490 that in fact they may need some additional cross-training because of the unique characteristics of this, quote, device mimicking an array of pharmaceutical drug and not operating as a true sealed source in the manner in which they are used to dealing with.

And I can speak for ACR that we would be willing to work with SNM and help the NRC define some perhaps additional criteria for this issue.

MR. UFFELMAN: And I would even invite ASTRO to sit at that table with us.

MS. FAIROBENT: And as well the physicists.

MS. MCBURNEY: I think if you all could do

that and then maybe correspond by e-mail or something with me.

MR. UFFELMAN: Why don't we shoot for a response by June 30th. Is that reasonable for everybody? What does that do for your time line?

DR. HOWE: When we are talking about guidance, and we are talking about the website, then we have no deadlines. We have no public things we have to meet.

MR. UFFELMAN: I'm just thinking that SNM's annual meeting is 3-1/2 weeks or 4 weeks from now, which means that I get a whole herd together of people who are interested, and ACR folks will be there, and we could work with ASTRO to pick a day in New Orleans, and I will buy you lunch or something at Commander's Palace or something.

DR. AYRES: We have guidance out there now, and so it is not holding up anything, and if at all that guidance should be changed.

MS. MCBURNEY: Okay. One of the other major issues I guess in this is what goes into the written directive.

MR. UFFELMAN: I think that is the other thing that we can talk about.

MS. MCBURNEY: Yes, at the same time you

have entered on that. Okay. Is there anything else on microspheres that --

MS. FAIROBENT: Lynne Fairobent again. I would just like to also follow up. I think it is key -- you made a point earlier, and Donna Beth did, too, that right now we have two particular devices approved by the FDA.

And recognizing that there may be other similar things coming down, I think we all need to keep in mind if we can write the guidance as flexible as possible, or as generic as possible, then hopefully we don't have to revisit the broad areas in the next device approval or drug approval coming out in this area from the FDA.

DR. HOWE: I think it is probably going to end up like Bob's IVP. In other words, we are going to have the broad guidance, and then we are going to have the specific unique part for each one coming down that is different.

MS. MCBURNEY: Right. Okay. GliaSite. You heard the presentation on the guidance. Do you all have any comments on how the NRC is dealing with this modality, physician training as manual brachytherapy?

DR. EGGLI: I think it is where it belongs.

MS. MCBURNEY: Okay. And whether a team is

needed for this?

DR. DIAMOND: I'm sorry, Doug, but when you say you think it is where it belongs, do you mean we should keep it at 35.1000, or that we should move it formally into the manual brachytherapy?

DR. EGGLI: It should be managed as a brachytherapy.

MS. MCBURNEY: As a brachytherapy source.

DR. DIAMOND: Right.

MS. MCBURNEY: And the training experience for that.

DR. DIAMOND: Right. So the question was asked earlier in the day at what point do you take a new technology and perhaps move that to one of the recognized subcategories.

DR. HOWE: I think at this point that it is a little early, because we don't know how widespread this is going to be, because we have to come up with a new regulatory area for a liquid source, and so --

MS. MCBURNEY: It is not a true --

DR. HOWE: If we can't put -- and this is probably one of the things that I didn't mention. We take some new technology and we look through the regulations and see where it fits.

And our guidance is that if it does not fit

in either one place, we have to move it to 1000.

DR. DIAMOND: So from your discussion earlier today when you were discussing it in the context of sealed sources and devices, that is where you saw it?

DR. HOWE: The leaky source is the issue, and the fact that --

DR. DIAMOND: But you were not advocating moving it to that section?

DR. HOWE: No, but I am advocating that we are using the guidance in the manual brachytherapy because it fits very well with it.

MS. MCBURNEY: In general.

DR. DIAMOND: Okay.

DR. HOWE: But there are some particular things that don't fit.

DR. AYRES: An example of a new modality that went right or just plugged into the existing regulation didn't require moving the 1000 was Zevlin.

MS. MCBURNEY: Right.

DR. HOWE: We looked at that and we said we don't have to write any exemptions from even how you write the written directive to what you record on all your records that are dealing with radiopharmaseuticals.

You don't have to say anything, and it fits, but our guidance has been -- and we weren't sure what our

guidance was going to be. We didn't know whether if it almost fit we could grant one or two exemptions, or if it almost fit and one little piece was out, we would have to automatically move it to a thousand.

And right now our guidance is if even one little piece doesn't fit, it shifts to a thousand.

MS. MCBURNEY: Isn't there even a newer modality, where you have a seeping balloon.

DR. HOWE: Actually, I think Proxima is looking at putting a tube in that releases a chemotherapy agent, another port, and it releases a chemotherapy agent in the brain.

MS. MCBURNEY: Okay.

DR. NAG: Now, the MammoSite, which is manufactured by the same company, should have no problem in --

DR. HOWE: The MammoSite is a brachytherapy source, and it is a ridium, and it does not seem to have any unique parts other than it is in a catheter in a balloon. So I have not looked at it in detail, but I can't imagine it is not going to fit.

DR. NAG: And you attach an HDR.

DR. TRIPURANENI: If I may speak about Zevlin for a minute. It is more of a question. In our institution, our nuclear (inaudible) are somewhat

uncomfortable dealing with Zevlin, and I am pretty heavily involved in not only evaluating the patient up front, and basically working with the nuclear (inaudible) very closely, that doing the (inaudible) scan together, and then basically we decide what dose it is, and then he basically does it, and I follow the patient thereafter writing in there.

DR. HOWE: And my understanding is that we have a number of radiation oncologists that are using radiopharmaseuticals, and there is more of a crossover in that area than there is in the opposite direction.

DR. TRIPURANENI: Again, there are instances where nuclear medicine physicians are not adequately trained in actually diluting (inaudible) doses of radiation with monocolonal antibodies, and --

DR. EGGLI: I think it depends on how you define nuclear medicine physician. If you are talking about a diplomate of the American Board of Nuclear Medicine, they are all trained for this.

If you are talking about practitioners of nuclear medicine who have a different approach, some are trained and some aren't, but all Diplomats of the American Board of Nuclear Medicine are trained in therapeutic nuclear medicine as part of their training program.

However, not all other practitioners, and not all other certifications have the same training and experience in therapeutic nuclear medicine as Diplomats of the American Board of Nuclear Medicine do.

MR. UFFELMAN: In doing the process of care for Zevlin, I literally went out and surveyed everybody who had administered Zevlin up through October of last year, and found how many were actually nuclear medicine physicians, versus radiation oncologists.

And the thing that seemed to make nuclear medicine physicians uncomfortable was just the experience of administering a monoclonal antibody that isn't something that they have typically dealt with, and then the fact that it was a long infusion.

And by package insert, it was 10 minutes, and the experience was that the typical was 20 minutes, and we found that the more that they had done, the closer it approached 30 minutes just because,. and I won't go into why they said it did.

But it is a different thing for a nuclear -- a nuclear medicine physician who has been down in the basement looking at images for 10 years, and now suddenly is doing personal supervision administration, and sitting in the room administering this 20 minute infusion or whatever, is just something that they have not done.

DR. HOWE: And we looked at that, and we said, well, okay, there is a much longer infusion, but where in the regulations is the infusion in that addressed, and the answer is it is not.

The regulation is general enough to cover this. There are unique properties to it, but those unique properties do not make it pop out of 300 at this point.

DR. TRIPURANENI: Is it 300 or 390?

MS. MCBURNEY: Well, 300 is a use.

MR. UFFELMAN: And 390 is the training.

DR. TRIPURANENI: Thank you.

MS. MCBURNEY: Back to GliaSite, are there any other issues that we need to deal with on that? The contents of the written directive set with how it is in the licensing guidance and so forth?

(No response.)

MS. MCBURNEY: And the labeling?

(No response.)

MS. MCBURNEY: Okay. IVB. I think that has been around a while, the guidance on that.

DR. AYRES: It has gone through several iterations in fact during that point in time.

MS. MCBURNEY: And you have heard Dr. Ayres' presentation on that this afternoon. Were there any

further comments on users, presence of various team members?

DR. TRIPURANENI: Once again, it is a question for clarification for my own benefit. Was the 35.1000 when it was devised was looked at more as a placeholder temporarily until it becomes more of the standard of care and then moving to a different regulation, and if it doesn't quite fit into in any of the existing regulation, would you ever conceive that we are going to create a new regulation?

DR. HOWE: I think initially 1000 codifies how we used to license by line item materials that weren't specifically covered in the rest of them. And I think in some minds that there is a difference of opinion.

And I think you have to recognize that 1000 is other. There may be some -- right now we are looking at some pretty serious therapies in 1000. The next one down the line could be a no, never mind, trivial low-dose something or another that just does not fit into anything else.

So we could go from trivial to high risk, and then you have to think about the cost of regulation, and the number in the community out there that are using it.

So we may have some things that are in a thousand that may be in a thousand for 30 years. They may still be in 1000 because there isn't enough of a reason to go through rule making to codify.

There may be other things in 1000 that really take off, they get solidified pretty easily and quickly on what we are looking at, and they could immediately move into rule making.

So you have got a spectrum, and I think that is what people have to recognize.

DR. TRIPURANENI: The reason that I raised the question is when you look at the 35.1000 imaging technologies, that kind of leads me to believe that at some point once it becomes not so standard that actually then it would be moved into a different area.

If I can comment for a couple of minutes. I agree with Dr. Brinker that probably it is very hard to get the number of cases that are being done every year, but when you talk to the three vendors and try to get the best information you can get, it usually comes anywhere between 50 to a hundred-thousand patients a year that are actually getting vascular drug stents at this point in anywhere between 400 to 600 centers.

I think the drug stent has actually be approved for the de novo stenosis, I suppose, and

technically it shouldn't be used for the instant restenosis, but that has now approved us, the physicians, to do what we want to.

There are currently two protocols that are going on looking at the efficacy of drug eluting stents (inaudible), and I think once the protocols become randomized trials looking at the drug (inaudible) stents (inaudible) radiation therapy, and I think if the trial is passed that the patients are better served by using the (inaudible) stent because it is much easier. and a simpler procedure, rather than involving radiation therapy.

But that remains to be seen, and I suppose in the next 12 to 18 months, depending upon the results of those tests, they probably may have to come back to this, and if that does not quite work out, we probably may end up 50,000 to 70,000 patients a year.

The other estimate is that as we are starting to use the drug-eluting stents much more frequently, that the number of angioplasties are going to go up significantly because the cardiologists are a lot more comfortable (inaudible).

In fact, there is an estimate that it is probably going to be close to 2 million angioplasties by 2005-2006. I guess the next 12 months is going to tell

where brachytherapy is going to end up in the, I guess, end up in the armamentarium that we have in the medicine.

But I suspect that if the past experience is any guidance, with all the chemotherapy, every time we find a new chemotherapy drug, everybody says it is going to go (inaudible) business. We have not quite gotten out of that yet.

DR. AYRES: A comment on moving something out of 1000. I think it would take -- it is kind of a cost benefit thing I think from the NRC perspective. Rule making is terribly resource intense, and long, and what savings do we have, and there are savings in licensing when it is in rule space rather than guidance.

Guidance, while it is emerging, clearly gives some flexibility in adjusting for what you see. For example, a classic example is the old rules were written in '84, I believe, and for 10 plus years it was through guidance that gamma-stereotactic radiosurgery and high dose rate remote afterloading, and pulse dose rate and all of that, was regulated through guidance.

And so you could say it was like moving it out when we did the new Part 35 and put those two for the first time in the rule.

MS. MCBURNEY: And you have to multiply any kind of rule making that the NRC does throughout the 32

plus agreements.

DR. AYRES: I think it would take some -- it is not a trivial thing to do, and it would have to be a significantly good reason to do that.

MS. MCBURNEY: Lynne had a comment.

MS. FAIROBENT: Yes, Lynne Fairobent, ACR. I am a little disturbed only by this discussion of moving stuff out of Part 1000, because in fact during the rule making and the public workshops during the drafting of the rule, and even the public workshops prior to the final rule coming into effect in October, there was discussion.

And one of the points that the NRC was adamant in making over this process was it is not their intent to try to license by license condition, and that Part 1000 was in fact no envisioned to be a session of the regulation in which permanent licensing would be done in accordance with, because every Part 1000 criteria requires a license condition for that to go forward.

And therefore what I think I am hearing does give me some concern as I think it is a slightly different position being voiced than what was voiced during the development of the regulation with the intent of Part 1000 to do some initial expeditious licensing methodology until, one, experience was obtained on

something that, quote, didn't quite fit or was emerging.

But that eventually -- and that had never been defined in a time frame, granted, but that in fact those procedures or license situations would in fact be moved out of 1000, and so therefore license conditions didn't have to continue to be the mode of licensing.

And I think that is something that certainly ACR would like to have clarified by the staff if that position on what the intent of 1000 is has changed.

DR. HOWE: I think you have to just look and say, well, okay, what if we have got an emerging technology that is basically allocated out in the Borad-scopes, and there is only three limited specific licensees that are involved in it.

In that case, the Borad-scopes, they don't have to come in for an amendment under 1000. So the Borad-scopes are able to continue offering that because there is not a big demand for it.

MS. FAIROBENT: But you didn't need Part 1000 to do that? You did not need Part 1000 to issue three specific license conditions in any ase?

MR. LIETO: Borad-scopes have always been able to do that, even before 1000. So 1000 doesn't --

DR. HOWE: But 1000 just codifies how we used to do things by licensed conditions, and there may

be just a few limited specifics that are going to need a license condition to do it.

And the NRC may decide cross-benefit not to do rule making for a very small number.

MR. LIETO: And everything that has gone into 1000, there is no plan to get it out. It has gone there and the IVBT has been there for what, 2 or 3 years already.

MS. FAIROBENT: Well, technically only 6 months, since October 24th. In any case, the experience base is greater.

MR. LIETO: The experience base has been there, and the issue is also that if you look back at the National Academy of Science critique about the NRC, one of the biggest issues that came out was the issue about regulating by license condition.

And when Part 35 was proposed, the issue was that if it required -- I mean, if it is going to be a license condition for everybody that uses it, it should be in regulatory space.

Now what you are saying is, well, we don't want -- because it takes so much effort, we are not going to put it out there. We are going to go back to the old methodology, and I think you are going to start to go down a slippery slope again.

And in a few years, you are going to be back to where you were, and you are going to be under a lot of criticism for it.

DR. HOWE: I think if the IVB stays at its current level and grows, it is probably going to be a prime candidate to move into regulatory space. But if the drug stents come in and they take the bottom out of IVB --

DR. NAG: Can someone explain what you mean by license -- I mean --

MR. LIETO: It is not in the regulations, but when you go to get a license, it is a condition of your license, and therefore it has the effect of law, but it never went through the regulatory process.

DR. AYRES: NRC licensing is permissive. In other words, if we don't say you can do it, you can't. So there has to be a way or needs to be a way, and there is, which is called license condition now, to authorize those things that are new that we can't cover.

So we can allow people to proceed with useful uses of byproduct material, even though we don't have a regulation covering or an authorization to grant that process through the regulation itself, but off the books if you will.

DR. NAG: Those are under 1000 and they

don't go through the regulatory process?

MS. MCBURNEY: They have to be added by a license condition for a limited scope license.

DR. AYRES: The guidance is advisory. Once it is written into the license between the licensee and the region who does the actual licensing, and becomes a license condition, then it has the same -- the licensee is expected to conform to their license conditions in the same manner that they conform to their rule requirements.

MS. MCBURNEY: And in order to get licensed, they have to agree to these --

DR. AYRES: But they are negotiable in a sense by guidance that they are not as rigid as my earlier talk about gamma stereotactic radiosurgery at present, and that is a requirement. There really isn't much wriggle room there.

There is wriggle room to the extent that the licensing reviewer wishes to use it, and they have latitude therein working out these license conditions.

DR. HOWE: Right. And we are not saying that we won't go to a rule making decision. That is a decision that management will have to make.

MS. MCBURNEY: I had a question of staff. I know that these were the first three items that you wanted input on. Are there any others that you see on

the horizon that are among the members of the Committee, are there other modalities that will come in under 35.1000 that you all see as potential for our subcommittee to provide input on?

DR. HOWE: You guys out in the borad-scopes, what do you see?

MS. MCBURNEY: What is happening?

DR. EGGLI: Well, there are going to be more and more therapeutic radiopharmaseuticals/devices coming down the line, and I think over time that you are just going to -- this is the direction that nuclear medicine, which has renamed itself to molecular imaging and molecular therapy, that is the direction that the whole field is moving out of many traditional imaging applications, and into some therapeutic applications.

So I think that although I can't tell you which ones are coming, I can tell you that like night follows day that there are going to be more of these kinds of therapy situations that are going to not quite fit nicely into a category, and I think we just need to be prepared to think about those as they get to a point where they begin to look like they are potentially promising on a clinical basis.

I mean, Bexar is on the verge of approval, and there is dosimetry associated with Bexar

administration. There is probably going to have to be --

DR. HOWE: What is Bexar?

DR. EGGLI: It is a monoclonal antibody to treat lymphoma, and similar to Zevlin.

MR. UFFELMAN: It is Zevlin with iodine.

DR. EGGLI: It is I-131. But there may be things that don't quite -- you know, that was the next one on the horizon. It is probably not a good example, because it probably will go into 300 nicely.

But there will be more things that may straddle categories, and I think that is where you are going to need to be prepared to act.

DR. HOWE: I think as long as you are staying in the biologic center and the drug center, those probably won't need to go into 1000. It is the stuff that is going to be --

DR. EGGLI: Well, delivery devices are probably going to get to be --

DR. HOWE: Yes.

DR. EGGLI: And there will be unique delivery devices with these new concepts, and I think that is where you are going to get involved and you may not have a clear definition of where every one of these things belongs.

DR. HOWE: Right. And I think there may be some devices that will have radioactive materials attached to them, and in the past the concept was the radioactive material stays on the device, and the future will be they are meant to move off of the device.

DR. EGGLI: Right, once they are delivered to their target. There was one more comment though if I might on the Brachytherapy. Do we need to address the public comments? There were a pile that Angela sent to us, a pile of public comments on the intervascular brachytherapy question. Do we need to address those anywhere?

That's where ASTRO had a statement, and some cardiologists had a statement, I guess. If we are going to address those, I would like to ask Jeff what is the role for emergency intervascular brachytherapy in the coronary artery.

DR. BRINKER: Right. And just to put some things in perspective. There is this big evolution or revolution right now concerning the role of the drug-eluting stents for instant restenosis is what was for de novo angioplasty.

And I think the biggest driving force for the drug-eluting stents after all is said and done is the fact that it can be done at the point of service without

the logistical requirements that accompany intervascular brachytherapy.

There have only been two pilot randomized -- not randomized, but registry studies really that looked at drug-eluting stents for instant restenosis, one of which was relatively good.

Only one restenosis, and no acute problems. The other one had three major complications out of 11 patients, and that was the one done by Cyrise (phonetic) in Holland.

They were high-risk patients, in terms of -- I think 2 of the 3 that had a problem had previous radiation therapy, and the other one had a huge long area of stenting.

It is not clear that drug-eluting stents are going to replace intervascular brachytherapy, but it is likely that for urgent situations they will be the fallback procedure until a definitive clinical trial is reported.

Now the reality is that in many places, including my own place, we have severe restrictions in our abilities to do -- I am stuck with coverage two afternoons a week.

And if a patient comes in -- you know, not totally emergent with a mild myocardial infarction, but

somebody with unstable angina, comes in on a Sunday, I might not get to them until Wednesday.

Or I have the choice of doing the procedure without radiation backup. Our radiation oncologist reached the position where they asked us if we wanted to go to the situation where we only have a physicist and the interventional cardiologist, because there were radiation oncologists in the group that didn't want to cover intervascular brachytherapy.

There is going to be a change at our place in radiation oncology, and we are waiting to see how that falls out, but I can tell you that nationwide, because we did a survey about this, that the logistical requirements as they were originally written were burdensome, and a lot of patients who could benefit from radiation aren't getting it.

Now, having said that, I think that there is -- the cardiology community was happy with the idea that most places where it was very problematic that the guidance had expanded to allow with everybody's approval.

I mean, the concept is still a team concept, and if the radiation oncologist brought into at a given site did not have the physical presence of that individual has been I think a big help in some centers.

It certainly is far from being universally adopted. There are a couple of issues on why I am sort of happy that we still have this in the 1000 area, because number one, if drug-eluting stents is a failure for instant restenosis, and it seems like intervascular brachytherapy is going to assume a relatively large burden, in terms of the business that the interventional cardiologist has to do, either the cardiology people would probably seek some sort of limited authorized user status by developing some sort of training and experience guidelines.

I hope personally that it doesn't come to that, and I don't think it will. But I think that this is one reason why I think that this is still an evolving area.

The other thing is that maybe you know more than I do. I know that there are at least two technologies. One was a radiation dose balloon basically, a film on a balloon, that would dramatically change at least the practice of intervascular brachytherapy.

I don't know whether that has been dropped or whether that is going to continue in some way, shape, or form; or maybe in the drug-eluting stents fail,

whether that would be a rebirth because of the issues involved.

But I think they are still nebulous enough to leave it at that.

DR. EGGLI: Does this committee need to make any recommendation to the NRC staff with respect to the regulations then or not?

DR. BRINKER: I think I am content, and most cardiologists that I know are content with the way that things lie here until we know which way things are going.

We also are testing -- not we, but the interventional radiologists are testing the application of this, and then larger vessels and using other issues. And there, their interests will also have to be lent an ear. So things are changing enough for us to ask that we keep where we are until --

DR. EGGLI: So we should put in our minutes that ACMUI evaluated the public comments and feel that no change is appropriate at this time?

DR. BRINKER: I feel --

DR. DIAMOND: No, no, we didn't say that. We had no discussion.

DR. AYRES: It sounds to me like what you agreed to is -- it sounds like you are agreeing that it is still an emerging technology. That was the main point

there.

DR. DIAMOND: No, no. I think the only reason, for example, to keep manual gamma vascularbrachy therapy in 1000, the only logical reason is simply that it costs some money to put in the 490s perhaps. There is no other logic behind or there is no other logic that I can conceive of by keeping the corner system under the 35 Subpart 1000. None.

So I would want to specify that. I also would want to go on record by saying that I would feel extraordinarily uncomfortable at this point with there being any sense that there is a movement amongst this committee to go and extend authorized user status to the interventional cardiologist community.

I mean, that is Jeff's personal opinion, and I respect Jeff and his thoughtfulness, but certainly I don't want --

DR. EGGLI: But that is not the current status quo.

DR. BRINKER: And I didn't say that there was a movement to extend this to interventional cardiologists. I said that in conditions, if things don't go the way that we suspect, we might apply for an authorized user status with whatever restrictions, and training, and educational and experiential requirements

are thought necessary for us by the NRC in order to accomplish this.

And of course we would almost assuredly ask for only beta application. The only issue about -- you know, you fall back on the gamma device, the only issue about the gamma advice is why not put that in brachytherapy now.

It sort of disrupts perhaps prematurely practice in those places that have either gamma or gamma and beta, as opposed to both and only beta. And I don't see the point in moving it right now.

It may in fact go away, and that is the least-used of all of the intervascular brachytherapy devices.

DR. AYRES: And Cordis has come in and demonstrated to us a remote afterloader for those, and if they did that, and it has been about a year and I have not heard anymore about their plan, but that one would plug right in to 600.

MS. MCBURNEY: Right.

DR. AYRES: It would be a perfect fit. So it isn't that that is not stable according to the company either.

DR. TRIPURANENI: I have done personally close to 600 to 700 intervascular brachytherapies, and in

our institution, we have done close to 1,600. We have used all three systems from the very beginning, dating back to 1995, and even today we continue to use three systems.

And I caution people that actually use one system only and have tried to come to conclusions that it is actually very dangerous. In fact, of all the three systems they used are actually more (inaudible) to betas being given away.

Gammas is something that you can measure with a dosimeter and actually see what is going on, but I think that with beta, one needs to be extra careful and we keep hearing that one device keeps on getting stuck, et cetera, right in there.

So I think any part of actually giving (inaudible) status is fraught with problems. So I hope that we have not constrained that. Just to answer Dr. Brinker's quickly.

The Radiants Company has actually folded, and research is actually completely shut down. And radioactive balloons, this part of the company was actually sold out to somebody that is actually not in research at this point in time.

The other thing that actually was interesting was an x-ray generator that actually you

could pass into the carotid artery. That was actually shut down.

Cordis actually pulled the plug on the remote afterloader for (inaudible) 192, and also to add one more trial. There was one more trial by the name of Taxis-3, using a Taxol Cordis stents for the instant restenosis, and also that turned out to be not useful in patients with instant restenosis.

So I submit to you that I think more than likely that intervascular brachytherapy is here to stay. And as it is said, it is not over until it is over. Once again, I would like to remind the point that I think that whether you believe Dr. Brinker or myself, it doesn't matter.

We have treated more than 100 to 300,000 patients in the States, and I expect that it will probably continue to be news for a while to come at least until something else comes along, possibly in relation to drug Cordis stents.

I think at some point that we do need to tap on the experience of what we have accumulated in the past several years, and then move on into some other group or whatever that may be new.

One last question for me is does anybody have a sense of what percent of patients are actually

being treated by the delegation of the authority of the authorized user to either AMP or the (inaudible)?

DR. DIAMOND: Well,I can tell you at our center that it is zero. I have not seen any surveys done regarding that issue.

DR. TRIPURANENI: Well, ASTRO conducted a survey, and I talked close to 30 to 40 centers in the country, and I have not heard of any of those -- and obviously I am talking to a limited group of people, and so it can't be generalized, but after close to 40 centers that I talked to, none of the authorized users are actually delegating their authority, even though they are given the permission to actually do that legally.

DR. BRINKER: Well, I can tell you that such exists. I don't think it is more than perhaps 10 percent, and I am not -- I mean, I think there is some degree of conflict here that is not necessary, because I don't think we know all of the answers. We are not asking for anything more than is already on the table.

And I think that we have to see where things go. I can tell you though that if the drug-eluting stents fail, things will be a lot different than if they are successful. And the mode of approaching them must be different.

And I will remind David that in our

discussion about authorized -- delegating the potential for the authorized user to the AMP, you actually supported that in our discussion a year or so again, whenever that occurred.

And even contemplated the possibility that you might have to use that yourself on occasion. So I think that we are happy the way that things are, and we can save the rhetoric until something really happens.

MS. MCBURNEY: It is about five o'clock, and are there any closing comments? Tom?

DR. EGGLI: Just a request. We have four papers or slides to present to the Commission next week. We have got to have your slides by tomorrow at the latest. We have already been asked for a briefing by the Commission technical assistance, and so it would be much nicer if we had the slides in-hand when we went there to talk with them.

MS. MCBURNEY: Yes, sir. And the input from the stakeholder groups on the issues that we discussed by July 1st to me and to Angela. Does everybody have my e-mail address?

DR. HEVEZI: Yes, I do.

MS. MCBURNEY: Okay. All right. I want to thank everybody for their input; the committee members, the staff, and you have done a tremendous job, and all

the stakeholders that were here this afternoon. Thank you.

(Whereupon, at 5:01 p.m., the closed session was recessed.)