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UNITED STATES OF AMERICA

NUCLEAR REGULATORY COMMISSION

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MEETING

ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

(ACMUI)

+ + + + +

OPEN SESSION

+ + + + +

WEDNESDAY

OCTOBER 13, 2004

+ + + + +

ROCKVILLE, MARYLAND

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The meeting came to order at 8:00 a.m. in
 Room T-2B3 of Two White Flint North, Leon S. Malmud,
 M.D., Chair, presiding.

COMMITTEE MEMBERS:

- | | |
|------------------------|----------|
| LEON S. MALMUD | Chairman |
| EDGAR D. BAILEY | Member |
| DAVID DIAMOND, M.D. | Member |
| DOUGLAS F. EGGLI, M.D. | Member |
| RALPH P. LIETO | Member |
| SUBIR NAG, M.D. | Member |
| SALLY W. SCHWARZ, RPh | Member |

1 COMMITTEE MEMBERS: (CONT.)

2 ORHAN H. SULEIMAN, Ph.D. Member
3 WILLIAM VAN DECKER, M.D. Member
4 RICHARD J. VETTER, Ph.D. Member
5 JEFFREY WILLIAMSON, Ph.D. Member

6 NRC STAFF:

7 THOMAS H. ESSIG Designated
8 Federal Official
9 Linda M. Gersey NMSS/IMNS
10 Patricia K. Holahan, Ph.D. NMSS/IMNS
11 Merri Horn NMSS/IMNS
12 Donna-Beth Howe, Ph.D. NMSS/IMNS
13 John Jankovich NMSS/IMNS
14 Andrea Jones RES
15 Charles L. Miller, Ph.D. NMSS/IMNS
16 John Szabo, Esq. OGC
17 Sami Sherbini, Ph.D. NMSS/IMNS
18 Sandra Wastler NMSS/IMNS
19 Angela R. McIntosh NMSS/IMNS
20 William Ward NMSS/IMNS
21 Ronald E. Zelac NMSS/IMNS
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P-R-O-C-E-E-D-I-N-G-S

1
2 MR. ESSIG: Good morning, ladies and
3 gentlemen. As Designated Federal Official for this
4 meeting, I am pleased to welcome you to Rockville for
5 the Public Meeting of the Advisory Committee for the
6 Medical Uses of Isotopes. My name is Thomas ESSIG.
7 I am Chief of the Material Safety and Inspection
8 Branch, and have been designated as the Federal
9 Official for this Advisory Committee in accordance
10 with 10 CFR Part 7.11. This is an announced meeting
11 of the committee. It is being held in accordance with
12 the rules and regulations of the Federal Advisory
13 Committee Act and the Nuclear Regulatory Commission.
14 The meeting was announced in the August 27th, 2004
15 edition of the *Federal Register*.

16 The function of the committee is to advise
17 the staff on issues and questions that arise on the
18 medical use of byproduct material. The committee
19 provides counsel to the staff, but does not determine
20 or direct the actual decisions of the staff or the
21 commission. The NRC solicits the views of the
22 committee and values them very much.

23 I request that whenever possible, we try
24 to reach a consensus on various issues that we will
25 discuss today and tomorrow, but also I value minority

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1 or dissenting opinions. If you have any such
2 opinions, please allow them to be read into the
3 record.

4 As part of the preparation for this
5 meeting, I have reviewed the agenda for members and
6 employment interests based on the very general nature
7 of the discussion that we're going to have today. I
8 have not identified any items that would pose a
9 conflict; therefore, I see no need for an individual
10 member of the committee to recuse themselves from the
11 committee's decision making activities. However, if
12 during the course of our business you determine that
13 you have some conflict, please state it for the record
14 and recuse yourself from that particular aspect of the
15 discussion.

16 At this point I would like to introduce
17 the members who are here today; Dr. Leon Malmud, who
18 is Vice Chairman of the Committee, who today is Acting
19 Chairman of the Committee in the absence of Dr. Manuel
20 Cerqueira. Mr. Edgar Bailey, who is the State
21 Representative. This is Mr. Bailey's first meeting.
22 He replaces Ruth McBurney from Texas. Dr. Douglas
23 Eggli, who is our Nuclear Medicine Physician; Dr.
24 David Diamond, one of our radiation oncologist
25 physicians; Dr. Subir Nag, a second radiation

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1 oncologist physician; Ms. Sally Schwarz will be here
2 momentarily. She was delayed. She's our Nuclear
3 Pharmacist Representative; Dr. Richard Vetter, our
4 Radiation Safety Officer; Dr. Jeffrey Williamson is
5 our Therapy Physicist; Mr. Ralph Lieto, our Nuclear
6 Medicine Physicist, and Dr. Orhan Suleiman, who is our
7 FDA Representative from the Center for Devices and
8 Radiological Health. As I mentioned, Committee
9 Chairman, Dr. Manuel Cerqueira was unable to attend
10 this meeting due to a conflict in his schedule which
11 he could not resolve.

12 Committee Member, Dr. Robert Schenter, who
13 is our newly appointed Patient Advocate Representative
14 and replaces Ms. Nicki Hobson, was unable to attend
15 the meeting due to illness. Dr. William Van Decker,
16 a Nuclear Cardiologist, who is seated at my immediate
17 left, will replace Dr. Cerqueira in that role as a
18 member of the committee.

19 So in the absence of the ACMUI Chairman,
20 Dr. Leon Malmud, ACMUI Vice Chair, will conduct
21 today's meeting. Following discussion of each agenda
22 item, the Chair, at his option, may entertain comments
23 or questions from members of the public who are
24 participating with us today. Dr. Malmud, please.

25 CHAIRMAN MALMUD: Thank you, Mr. ESSIG.

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1 The next item on the agenda is the radio immuno
2 therapy and microsphere therapy discussion, which will
3 be presented by Dr. Donna-Beth Howe. Dr. Howe.

4 DR. HOWE: Thank you, Dr. Malmud. We've
5 gotten questions at a number of the ACMUI meetings
6 about how we regulate the monoclonal antibodies and
7 the Yttrium- 90 microspheres. And Dr. Nag especially
8 wanted us to clarify again how we're regulating these
9 things, so I've prepared a number of slides. They're
10 in your book, and what you'll see is a lot of slides.
11 But there's a section that says "Background", and
12 after Background, what I've done is I've just repeated
13 what's in the regulations so that if you wanted to
14 look at the regulations, they would be right there and
15 available at your fingertips.

16 Okay. The first thing I need to do is to
17 kind of clarify the question of emerging technologies
18 for 35.1000 uses, which is other medical uses. And
19 the way we determine whether something falls into
20 35.1000 is that we have to first determine that it
21 does not fall into one of the other categories.

22 If it almost fits into one of the other
23 categories, but misses by a small amount so that we
24 would have to have additional requirements for
25 radiation safety or we would have to grant an

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1 exemption from a requirement, then that will
2 automatically throw the modality into 1000. And
3 that's a key point to remember here.

4 A lot of times something that is a new
5 technology for the medical community may be something
6 that we already have adequate regulations for, and so
7 the medical community may think well, I've got a new
8 technology, and why isn't NRC developing guidance on
9 it. And the reason may be that we already have an
10 adequate regulatory structure to handle that
11 particular modality. So what I'm going to do is I'm
12 going to kind of go back and forth between the
13 monoclonal antibodies and the Yttrium- 90
14 microspheres, and kind of show the similarities and
15 the differences, and how we arrived at where we're
16 regulating them.

17 The first thing to note is that for the
18 radio immuno assay, the monoclonal antibodies, first
19 of all, FDA regulates them as radioactive biologics,
20 which is a subset of radioactive drugs. So they are
21 listed for manufacture and commercial distribution
22 under 35.72 or equivalent state regulation, so
23 they're coming through the drug side of our
24 regulations.

25 They are clearly a medical use, so they're

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1 going to be under 35. They are a therapeutic
2 procedure that requires a written directive. So the
3 next thing to do is -- so that's the basis on which we
4 start with the monoclonal antibodies.

5 If I want to look at the Yttrium- 90
6 microspheres, first of all, FDA regulates them as
7 medical devices. They are sealed sources. They are
8 listed in our sealed source and device registry. They
9 are licensed for manufacture and distribution,
10 commercial distribution under 35.74. The
11 radiopharmaceuticals come under 32-72. 35.74 is an
12 error, it should be 32-74. So the pharmaceuticals
13 come under 32-72, the devices come under 32-74. Once
14 again, they're a medical use. They're again a
15 therapeutic procedure that requires a written
16 directive. So how do we use this?

17 Both of them are therapeutic procedures
18 that require written directives. I go to the
19 regulations and I look at what part of the subparts of
20 the regulation 35 require written directives; unsealed
21 byproduct material, manual brachytherapy, photon
22 emitting remote afterloaders, teletherapy and gamma
23 knives, and then Subpart K. If I want to use the
24 radio immuno therapy, the one that comes under drugs
25 would be the unsealed byproduct material. And in

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1 that, you'll see in 35.300 that it has to be
2 manufactured by somebody under 32-72, or the
3 authorized nuclear pharmacist can prepare it. So the
4 monoclonal antibodies do come through that route.
5 They're regulated as drugs. They come through the
6 manufacture and distribution system correctly. And
7 then you look at the other requirements in Subpart E
8 and you'll find the monoclonal antibodies fit very
9 nicely into 35.300, and all of the requirements that
10 go with 35.300.

11 If you look at the microspheres, they're
12 devices, and you look at the unsealed byproduct
13 material. They're sealed byproduct material, so they
14 don't fit under E. Manual brachytherapy, sealed
15 sources, manual brachytherapy - if you look at the
16 microspheres, they are manual brachytherapy sources,
17 but they're really tiny. They aren't afterloaders,
18 they aren't teletherapy, they aren't gamma knives.

19 Now in manual brachytherapy - when I look
20 at the requirements for manual brachytherapy, there's
21 some requirements in manual brachytherapy that the
22 microspheres just cannot meet because of their very,
23 very small size. You can't count them. You can't
24 keep counting the way you would for other manual
25 brachytherapy sources, so we would have to give you

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1 relief from the regulations. That automatically
2 throws it into 35.1000. You cannot fit the
3 microspheres exactly into manual brachytherapy.

4 There is some discussion, well, you can
5 put them in like radioactive drugs. It's like the
6 microaggregated Albumin. Well, the microaggregated
7 Albumin comes through the commercial distribution
8 system under 32-72, which is your commercial nuclear
9 pharmacies, and your drug manufacturers, and federal
10 facilities that are neither drug manufacturers or
11 commercial nuclear pharmacies, so you'd have to grant
12 an exemption from that.

13 It's not a drug. Everything in 35.300
14 says you will handle drugs this way. You would need
15 exemptions from all of those parts, so it clearly is
16 not a 35.300. It fits much better in the 35.400 with
17 very minor adjustments.

18 Now the other thing that you have to
19 consider is that you have regulations that are
20 appropriate to all parts that are used under 35, and
21 so one has to go through the Subpart A - General
22 Information; B - General Administrative Requirements;
23 C - Technical Requirements, and you look to see those
24 parts that pertain to in this case 300 uses or 400
25 uses to see if there's anything in the 300 uses that

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1 the monoclonal antibody cannot meet, and you find
2 there's nothing in the 300 uses that the monoclonal
3 antibody use cannot meet. So it fits perfectly into
4 300, so NRC has not developed any new guidance for the
5 use of monoclonal antibodies, because we consider
6 monoclonal antibodies to be clearly under 300.

7 Now you look at the microspheres, and you
8 look at the general information, administrative - and
9 you find that there are a few minor parts that would
10 need exemptions because they don't fit exactly in
11 there. And once again, it's because of their very
12 small size, and the fact that you cannot count these
13 things. Well, the leak test is okay because the
14 activity for each seed is well below the leak test
15 limit, so you don't have to do a leak test, so it fits
16 that part of manual brachytherapy. But generally, it
17 is how you count these sources, and how you account
18 for them. You would need an exemption, so it fits
19 over in the 1000 category, and that just supports the
20 idea that this is a 35.1000 use.

21 And then we developed guidance for the
22 35.1000 use, and to assure that we have as close to
23 risk-informed performance-based as we can get, we
24 adopt those parts of the regulation that fit this
25 other category without any change, and we say you,

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1 licensee, just need to commit to follow those parts of
2 the regulation, so we tell them in the guidance to
3 commit to following the 35.400 requirements in the A,
4 B, C reports and also in Subpart I think it's F. And
5 then we add additional requirements or relief, as the
6 case may be, to fit this particular device. And
7 that's why we tell the licensee they don't have to
8 count the sources. They can use activity. We try to
9 put other guidance that will be helpful, and unique to
10 this particular type of device. So that's how we get
11 to where we are.

12 Our conclusion is that the monoclonal
13 antibodies are clearly regulated under Subpart E,
14 Unsealed Byproduct Material, Written Directive
15 Required - no new guidance. We conclude the Yttrium-
16 90 microspheres are regulated pursuant to Subpart K,
17 the medical uses.

18 Now the major concern was how does the
19 radiation oncologist use the monoclonal antibodies,
20 and the answer is that right now the radiation
21 oncologists can use the monoclonal antibodies, and
22 they use it either by the Board certification route in
23 35.930 or the alternate pathway in 35.930. And that's
24 because we have essentially taken the alternate
25 pathway for I-131 use and adapted it for every other

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1 type of therapeutic Isotope. So if you required 80
2 hours of training and experience and three cases for
3 I-131 use, we have by policy said if you're going to
4 use any other therapeutic radio pharmaceuticals under
5 Subpart J, you get 80 hours of training and experience
6 pertaining to that pharmaceutical, and you use three
7 cases pertaining to that Isotope and that
8 pharmaceutical. So that's how we have expanded 300
9 which has training and experience specifically for I-
10 131 into the Strontium-89, into the Yttrium-90
11 microsphere, I mean not microspheres but monoclonal
12 antibodies. That's how we've expanded into those new
13 isotopes that are being used for therapy that didn't
14 exist when the original 300 was developed way back in
15 the early 80s.

16 MEMBER WILLIAMSON: That's in the current
17 Subpart J?

18 DR. HOWE: The current Subpart J. But the
19 current Subpart J, and I've got the current Subpart J
20 in the backup slides, so you can see the boards that
21 are listed there.

22 MEMBER DIAMOND: Excuse me, Donna-Beth.

23 DR. HOWE: Yes.

24 MEMBER DIAMOND: There's a discrepancy
25 between the slide and the printout. It's Board

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1 certification route in 35.930, and alternate pathway
2 in 35 --

3 DR. HOWE: No, 930. 390 requires you to
4 --

5 MEMBER DIAMOND: Here it says 390.

6 DR. HOWE: Oh, the handout - then I must
7 have made a correction. Sorry. So you need to mark
8 it out.

9 MEMBER DIAMOND: So it's 930 for both.

10 DR. HOWE: 930 for both, yes. And the
11 reason it's not 390, is 390 requires 700 hours that
12 are appropriate for therapeutic radio pharmaceuticals
13 only, and it's easier to come through the 80 hours of
14 training than the 700 hours, so most people are coming
15 through this way.

16 Okay. Now the next question is, were the
17 radiation oncologists qualified to be authorized users
18 under 390. And I can only talk in the public meeting
19 about the proposed rule that is out to the public. I
20 can't talk about what the staff is doing to revise it.
21 And the answer is that for the Board certification
22 route, probably not. It's hard to imagine that the
23 Radiation Oncology Boards that are traditional for
24 radiation oncologists will include 700 hours of
25 classroom and laboratory training in unsealed

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1 byproduct material. Yes.

2 MEMBER WILLIAMSON: I understand from this
3 morning's closed meeting we can, in fact, discuss
4 predecisional documents in a public meeting. Is that
5 not correct, Tom?

6 MR. ESSIG: Yes.

7 DR. HOWE: Can they discuss the specifics
8 of what they've seen that hasn't been distributed to
9 the public? Okay. The staff is working on a solution
10 that would -- let me get to the next slide. On the
11 alternate pathway, probably not, but the staff is
12 working on the solution.

13 MEMBER NAG: I think here is where we had
14 been talking about the fact that the 700 hours
15 overlaps, and then when you've had 700 hours of
16 overall radiation training, does not require an
17 additional 700 hours of unsealed byproduct training,
18 because most of the body of knowledge is the same, and
19 you just need to apply that knowledge. So I think
20 when you talk about the 700, we do not have to say 700
21 for sealed product, 700 for unsealed product, and they
22 are separate. They consider the overall radiation
23 safety problem.

24 DR. HOWE: In the training and experience
25 for the 35.390, it specifically says 700

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1 classroom/laboratory in unsealed byproduct material --

2 MEMBER NAG: When you --

3 DR. HOWE: The staff is working on a
4 method that - I can't address it too much, but the
5 staff is working on a method that Roger will talk
6 about tomorrow, that says we recognize this was a
7 problem in the proposed rule, and the staff has worked
8 on the solution, so that was a major concern.

9 MEMBER WILLIAMSON: Is this the 35.396
10 rule?

11 DR. HOWE: Yes, it is.

12 MEMBER WILLIAMSON: Okay.

13 DR. HOWE: Yes, it is. Okay. And we
14 can't say what it is?

15 MEMBER DIAMOND: This is a major issue.
16 We're going to have to go and figure out how we're
17 going to have meaningful conversation on this.

18 MR. MILLER: We can have discussion on
19 this issue. It's just that we cannot hand out any
20 documents because any documents would be
21 predecisional.

22 MEMBER WILLIAMSON: Well, I think the
23 whole discussion, including Subir's presentation,
24 would be a lot more meaningful if someone would give
25 a concise summary of what 396 says.

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1 MEMBER NAG: Yes, but could we do it after
2 I give my presentation, because many of the things
3 will overlap in my presentation, so do you want to
4 discuss after that or before that?

5 DR. HOWE: Do you want me to give an
6 overview of what 396 is?

7 MR. MILLER: I think Dr. Nag's got a
8 question on the table for the committee.

9 MEMBER NAG: I'm going to be talking on
10 many of the issues from the clinician standpoint.
11 She's talking from another standpoint, and maybe some
12 of the discussion may take place after both our
13 presentations are made, or do you want to do it
14 before?

15 CHAIRMAN MALMUD: My preference as Chair
16 would be to have both parties given the opportunity to
17 make their presentations first, and then have a
18 discussion, if that's agreeable with the other members
19 of the committee.

20 DR. HOWE: They've indicated I can give
21 you a brief synopsis of what's in 396.

22 CHAIRMAN MALMUD: Please do.

23 DR. HOWE: Okay. The whole purpose of 396
24 was to provide a pathway for radiation oncologists to
25 be able to use radio therapeutic drugs. One criteria

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1 is that you already be recognized as an authorized
2 user for 35.400 uses and 600 uses. The second was in
3 case that you were board certified in one of the
4 boards recognized for 35.400 use or 35.600 use, so
5 that's specifically for the radiation oncologists.
6 The nuclear medicine type physicians can come in under
7 390 and meet those criteria.

8 The next thing was that the radiation
9 oncologists do need training and experience in
10 unsealed material. And just as Dr. Nag said, do they
11 need the whole 700 hours? The staff didn't think so,
12 so the staff looked at the I-131 training and
13 experience requirements for hours, and for 392 and
14 394, and said this is probably a good level of
15 additional training and experience, or a block that's
16 in their normal residency training that would cover
17 the unsealed byproduct material, so that was set at 80
18 hours.

19 Then we also brought across the three
20 cases, and there's also a preceptor statement that
21 goes with the fact that the person now can function
22 independently in using these materials, and so the
23 whole purpose of 396 was to provide a pathway for the
24 radiation oncologist to continue to use the types of
25 materials that they have been using all along in a

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1 system that's very similar to what they've been coming
2 under previously. Most of them came the alternative
3 pathway, or the board certification, but it's unlikely
4 that the board certification pathways for the
5 radiation oncologists will meet the 700 hours of
6 training and experience that's specified in 390, so
7 this is an alternate pathway to address that issue.

8 CHAIRMAN MALMUD: Dr. Eggli.

9 MEMBER EGGLI: The qualifications for that
10 preceptor is that the preceptor has to be Part 3
11 preceptor.

12 DR. HOWE: I don't have the rule in front
13 of me, but I think it is someone that comes under 390,
14 because we want to make sure that the radiation
15 oncologist knows the rules and how to do things under
16 390 for that particular part.

17 CHAIRMAN MALMUD: Dr. Nag.

18 MEMBER NAG: Now what if the radiation
19 oncologist is the person who is developing some of
20 these new techniques. And that person will not have
21 a preceptor. Basically, he is his own preceptor.

22 DR. HOWE: You always have the problem of
23 the first person out of the block, but you're looking
24 for a preceptor that has experience with therapeutic
25 drugs, not necessarily that therapeutic drug, but

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1 therapeutic drugs under that category. And if you're
2 the person that's developing it, chances are you're in
3 a big hospital, and there will be somebody there that
4 can do that.

5 MEMBER EGGLI: Also, aren't these likely
6 to be prior licensed people whose radiation safety --
7 they just have a little bit more leeway as the first
8 adopters.

9 DR. HOWE: Yes. The probability of the
10 first one coming through anything under than a broad
11 scope licensee is pretty small - not unheard of, but
12 it should be pretty small, so you've got that built-in
13 mechanism that the Radiation Safety Committee for the
14 broad scope can do a safety evaluation for materials
15 and uses that have not been in existence before.

16 CHAIRMAN MALMUD: Dr. Howe, for purposes
17 of clarity, may I ask a question based on a concrete
18 example. Let's say that there is a hospital with a
19 broad license that has a radiation therapy department,
20 and a radiology department. And in the radiology
21 department is a section of nuclear medicine. The
22 section of nuclear medicine traditionally has offered
23 I-131 therapy, an unsealed source, for thyroid
24 disease. The radiation oncologists traditionally have
25 not offered that therapy. At this point, the

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1 radiation oncologist wishes to use microspheres.

2 What will be the steps required by this
3 board certified radiation oncologist, who has perhaps
4 10 or 20 years of experience in his or her specialty
5 to now provide therapy with microspheres?

6 DR. HOWE: That was my next one, the
7 microsphere therapy. The microsphere therapy is under
8 35.1000, and at this particular point we consider that
9 to be manual brachytherapy. And the training and
10 experience criteria for manual brachytherapy are the
11 radiation oncology ones. And your question was for
12 the --

13 CHAIRMAN MALMUD: For the radiation
14 oncologist to provide that therapy. And you say it's
15 already -- that that therapy would be under the 1000,
16 and that therefore, the radiation oncologist can go
17 ahead and provide that therapy.

18 DR. HOWE: Yes.

19 CHAIRMAN MALMUD: Now let's take the other
20 side of the question. How will the nuclear physician
21 or nuclear radiologist be authorized to use
22 microsphere therapy with --

23 DR. HOWE: Right now our guidance says
24 that we will consider the authorized user to be
25 qualified if they meet the criteria in 35.490 or

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1 35.940. But our guidance also says that this is one
2 way of meeting the criteria in 35.12. The licensee
3 can, if it's a limited specific licensee, they can
4 come in and they can propose someone else. And they
5 can provide their training and experience, and we will
6 evaluate it.

7 The ACMUI and the public have indicated in
8 the past that they believe that a nuclear medicine
9 physician that comes under the 35.390 route, not the
10 930 which is the I-131 route, but the 700 hours, the
11 big broad picture with experience in a number of
12 isotopes, and experience in a number of different
13 types of procedures in the therapy should be able to
14 use the microspheres. And so that's right now on a
15 case-by-case basis for the limited specific.

16 The broad scope licensee is supposed to do
17 an individual safety evaluation for any new uses or
18 new materials, or new uses of existing materials, and
19 we would hope that in their safety evaluation they
20 would do a careful review of who they will be
21 approving, and ensure that they have a broad range of
22 experience in a variety of radiotherapy drugs, and
23 then additional training that is pertinent to the
24 35.400 use aspects of the microspheres. Because all
25 the rules and regulations that go with the

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1 microspheres are over in the manual brachytherapy
2 side. Things that you may not normally deal with in
3 the 300 side; accountability, additional surveys, a
4 number of different items that are covered in the
5 regulatory space, 400. So our guidance says 490 now,
6 but on an individual basis with extensive training we
7 will consider someone coming through 390.

8 CHAIRMAN MALMUD: If I may, the use of the
9 term "extensive training" perhaps could be clarified
10 a bit more for us. An experienced nuclear radiologist
11 or nuclear physician who has traditionally offered I-
12 131 therapy for both hyperthyroidism and thyroid
13 cancer, who has occasionally in the past used P-32
14 therapy for a variety of disorders, now wishes to use
15 the microspheres. What does this board certified
16 experienced physician require by way of additional
17 training in the eyes of the NRC?

18 DR. HOWE: That's something we evaluate on
19 a case-by-case basis. If the board certification was
20 in an area that they got the additional therapy, not
21 because of the board certification, but because they
22 had the -- came the alternate pathway on the 300 use,
23 they were like a 200 nuclear medicine physician with
24 limited experience in I-131 for hyperthyroidism and
25 thyroid carcinoma, we would probably not approve that

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1 individual until they got additional training in beta
2 microdosimetry, the kinds of things you need to know
3 with this Yttrium-90 microsphere.

4 CHAIRMAN MALMUD: Even though that
5 physician may have been providing I-131 therapy on a
6 regular weekly basis to hundreds of patients over the
7 past decade?

8 DR. HOWE: The Yttrium-90 microspheres are
9 not the same as I-131.

10 CHAIRMAN MALMUD: I understand that.

11 DR. HOWE: And it's those differences that
12 we're concerned about in the training and experience.

13 CHAIRMAN MALMUD: So getting back to the
14 practical follow-up of my question which I'm trying to
15 clarify for the committee, what would such a
16 physician, a nuclear radiologist require in addition
17 to the board certification, the training in both
18 therapeutic and diagnostic uses of isotopes that were
19 given prior to his board certification, or her board
20 certification, and a decade or so of experience with
21 hundreds of cases treated with either P-32 or with I-
22 131. And where would that -- who would give that
23 training? Where would it come from?

24 Traditionally, new therapies are learned,
25 as you pointed out earlier, on a case-by-case basis,

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1 and then the physician gets approval to use these
2 through the hospital and it's own mechanism for
3 assuring patient safety. What would the NRC require
4 by way of additional training for this experienced
5 physician beyond that which he or she already has;
6 numbers of hours?

7 DR. HOWE: We don't put numbers of hours
8 on things, because it's based on the individual, and
9 that's something we've heard from the medical
10 community many times, is that numbers of hours is not
11 the right way to go. So it's more topics and
12 concepts, and so we would look for their training and
13 experience in the topics and concepts that are listed
14 in 490 that pertain to the use of the microspheres.
15 And those are different than those -- some of the
16 topics are the same in 390, some are different.

17 There are physicians out there that are
18 authorized users now in Yttrium-90, so we aren't faced
19 with a case of the very first physician, so there are
20 individuals that have experience in Yttrium
21 microspheres, and are authorized users that can be
22 used to help provide training either through vendor
23 organized training sessions or other means. So there
24 is the ability for an experienced Yttrium-90
25 microsphere person to provide training for --

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1 CHAIRMAN MALMUD: Rather than pursuing my
2 questioning, I see we've now stimulated some questions
3 from other members of the committee. Dr. Eggli.

4 MEMBER EGGLI: I think that radioactive
5 iodine may be the wrong model to look at from the 390
6 users. In fact, P-32 chromic phosphate, which is a
7 small particle pure beta emitter, which is used
8 routinely as part of 390 therapy may be a better model
9 for evaluating the ability of a physician certified
10 under Part 390 to do 300 therapies to look at that
11 kind of experience as more similar to the microsphere
12 experience, and look at the amount of experience the
13 individual has handling this particulate beta emitter
14 as some evidence of experience with a similar type of
15 treatment source. And I think I-131 is the wrong
16 comparison to make. I think particulate P-32 is a
17 more relevant comparison.

18 CHAIRMAN MALMUD: Thank you, Dr. Eggli.
19 Dr. Nag.

20 MEMBER NAG: Yes, I think the point I
21 would like to make is that for the Yttrium therapy,
22 there are two components. One is what is required in
23 terms of the physical injection and the radiation
24 safety and the spillage and so forth. That, I think,
25 is probably easier to be done. But the second aspect

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1 is that the person who is taking charge of the Yttrium
2 therapy has to have the knowledge of what is liver
3 cancer, how that liver cancer spread. It's not just
4 a matter of putting some radioactive material into a
5 tumor unless you know the behavior of the cancer. So
6 I think it requires both the knowledge of the cancer,
7 and how much radiation can be given. It's not just a
8 matter of injecting 2 millicuries or 3 millicuries,
9 because to be able to control that you need to know
10 when to stop. Should I stop after giving one
11 gigabecquerels or should I go on to 2 gigabecquerels.
12 So I think that's where this extra training that she's
13 talking about comes in. It's not that well, I know
14 how to handle iodine, and I know how to handle the
15 radiation safety part of that, but in addition you
16 have to know where does the cancer go. When you have
17 a backflow, does it backflow to the stomach? Do you
18 have a shunt into the lung and so forth? I think
19 that's the additional training that needs to be there
20 for someone to be practically using the Yttrium
21 microspheres.

22 CHAIRMAN MALMUD: Dr. Diamond.

23 MEMBER DIAMOND: Subir was starting to get
24 a little bit into the practice of medicine, and I
25 think that would be useful. We may have a little bit

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1 of a non sequitur. Perhaps it would have been useful
2 if Subir had done his presentation first, but I just
3 want to be very clear on a couple of points.

4 Let's first direct ourselves to
5 microsphere therapy. Microsphere therapy, Donna, if
6 I understand you correctly, will fall into a 35.1000
7 use because of the reasons you described.

8 DR. HOWE: Yes.

9 MEMBER DIAMOND: And the training and
10 experience that will guide AU status for that will be
11 35.490 or 35.940. Is that correct?

12 DR. HOWE: Yes.

13 MEMBER DIAMOND: Okay. With respect to
14 radio immuno therapy, that will be considered a 35.390
15 use.

16 DR. HOWE: A 35.300 use.

17 MEMBER DIAMOND: 35.300 use, and for the
18 radiation oncologist to qualify, it will either be a
19 board certification or alternate pathway under 35.930.

20 DR. HOWE: Right now it's under --

21 MEMBER DIAMOND: Right now.

22 DR. HOWE: -- 35.930, but when Subpart J
23 disappears, that pathway won't be available any more.

24 MEMBER DIAMOND: Right. And then you're
25 invoking that this would fall under 35.396.

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1 DR. HOWE: Yes.

2 MEMBER DIAMOND: Okay. Now in this 35.396
3 rule, there would be an alternate pathway for
4 radiation oncologists which would require the 80 hours
5 of laboratory and classroom, plus the three cases. Is
6 that what you said?

7 DR. HOWE: Yes.

8 MEMBER DIAMOND: Plus the attestation. Is
9 that correct?

10 DR. HOWE: Yes.

11 MEMBER DIAMOND: Now in addition to that
12 alternate pathway, my question to you is, for the
13 radiation oncology residents who are in training
14 programs, recognized training programs, when they go
15 to take their boards, hopefully pass their boards, at
16 that point that they receive board certification, will
17 that in and of itself qualify them to use radio immuno
18 therapy or not?

19 DR. HOWE: No.

20 MEMBER DIAMOND: Okay. Therein lies the
21 problem.

22 DR. HOWE: And that's something that the
23 rule language working group can work on, is that the
24 board certification for the radiation oncologist most
25 probably will not meet the criteria in 390, and that's

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1 the route that has the board certification.

2 MEMBER DIAMOND: So, for example, right
3 now the chromic P-32 is also a 390 use. Correct?

4 DR. HOWE: Yes.

5 MEMBER DIAMOND: Radiation oncologists
6 traditionally have been using that, as well.

7 DR. HOWE: And they come through the --
8 there are some boards that the radiation oncologists
9 have that are listed under 930, and then the alternate
10 pathway is the 80 hours and the three cases that we
11 have by policy adapted to all the other therapy
12 isotopes that are coming down the line, and not just
13 I-131. So they're coming basically through the
14 Subpart J path.

15 MEMBER DIAMOND: Okay. So as a pragmatic
16 issue, what I want to be clear upon is that those
17 residents coming through training who take their
18 boards and pass their boards, will de facto have the
19 opportunity to deliver these radioactive materials as
20 long as they have those three cases essentially. Is
21 that correct?

22 DR. HOWE: If their board is listed in
23 Subpart J right now.

24 MEMBER DIAMOND: The American Board of
25 Radiology, for example. Okay.

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1 DR. HOWE: It's listed in Subpart J.
2 That's true.

3 MEMBER DIAMOND: All right. That's the
4 pragmatic issue. The other issue is a issue that Dr.
5 Malmud has raised a number of times, which is this
6 definition of how the 700 hours classroom and
7 laboratory training is actually enumerated, because I
8 would still go back and argue the same case as Dr.
9 Malmud, which is, I believe the way that you are
10 accounting for those hours is not the same as the way
11 we would account for those hours, recognizing how
12 there is overlap in the different radio nuclide
13 experience and understanding of these properties.

14 DR. HOWE: I think the point is that we
15 recognize that in your three years of residency, you
16 get --

17 MEMBER DIAMOND: Four years.

18 DR. HOWE: Four years, you get a
19 tremendous amount of radiation safety, use of
20 materials. The focus is probably more on the sealed
21 sources and the devices, and the question in the
22 regulations is, are there enough hours in there on
23 unsealed material? And would the residency move to
24 700 hours in unsealed materials? And the answer is
25 probably no.

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1 MEMBER DIAMOND: See, the other issue is
2 that these training programs are not monolithic.
3 There's tremendous disparity on what an individual
4 resident's experience is. For example, where I
5 happened to train in St. Louis, we actually divvied it
6 up so that the diagnostic isotopes were delivered by
7 the nuclear medicine physicians, and all the
8 therapeutic uses were delivered -- therapeutic for
9 cancer, excuse me.

10 MEMBER WILLIAMSON: Yes. Benign versus
11 malignant.

12 MEMBER DIAMOND: Yes, that's a better way
13 - malignant indications were done by us. So with our
14 particular experience, we had huge experiences in the
15 use of I-131 for thyroid cancer, P-32 for malignant
16 uses, Strontium-89 for malignant uses, so someone
17 coming through that training program would easily
18 meet, I think, your 700 hours.

19 DR. HOWE: The question is whether the
20 board for 390 requires 700 of unsealed material. And
21 if the board doesn't require 700 of unsealed material,
22 then -- your program has it, and so you can use what
23 you had in your program to come under 396, and say in
24 my residency training I had way in excess of 80 hours
25 in unsealed material.

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1 MEMBER DIAMOND: Still, you'd have to go
2 through the alternate pathway.

3 DR. HOWE: You may decide that there's a
4 possibility there's a board that requires that of its
5 board certification members, and they suggest maybe
6 there would be a straight board route.

7 CHAIRMAN MALMUD: Dr. Nag.

8 MEMBER NAG: Yes. I think this is what
9 the 700 hours is being misinterpreted, I think. When
10 someone has gone for four years of training, and has
11 had more than 700 hours of overall therapy training,
12 you can extend many of those into unsealed versus
13 sealed, so that you don't need any of the 700 hours.
14 That's the point I was trying to get across.

15 The direct question I have for you is a
16 question similar to Dr. Malmud, and that would be if
17 a board certified radiation oncologist is now going to
18 do radio immuno therapy, having done iodine therapy
19 and other therapies, now want to do radio immuno
20 therapy, what other training would he or she need, or
21 would he need any further therapy?

22 DR. HOWE: For the existing radiation
23 oncologist, then NRC looks at 930, and they look at
24 the -- they either look at the board certification or
25 they look at the alternate pathway. And the alternate

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1 pathway says you have 80 hours of training and
2 experience in unsealed material requiring a written
3 directive, and you have three cases. So the NRC
4 license reviewer is going to say have you done three
5 cases in radiation therapy, because you're applying
6 for say metestrum or you're applying for monoclonal
7 antibody, and you worked under the supervision of an
8 authorized user to get your three cases, then NRC is
9 going to look at that and say okay, we're going to
10 apply the same criteria to you that we apply in 932
11 and 934, but specifically for those isotopes. And
12 yes, you meet it, so we'll list you as an authorized
13 user for 390, 300 materials and we may specify
14 excluding I-131 or whatever based on what your
15 training is and your three cases. So we look at that
16 and we say yes, and that's what we do right now, is we
17 go over to the Subpart J and we say yes.

18 MEMBER WILLIAMSON: So your 396 is
19 intended to be a reincarnation of that Subpart J
20 pathway in the revised regulation.

21 DR. HOWE: Yes.

22 MEMBER WILLIAMSON: So actually, the
23 procedure wouldn't change for most radiation
24 oncologists.

25 DR. HOWE: Yes. And if you believed there

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1 was a board that would require you to have the minimum
2 hours of unsealed byproduct material needing a written
3 directive, that could be added to 396 too.

4 MEMBER DIAMOND: So extant radiation
5 oncologists, extant board certified radiation
6 oncologists, would they be grandfathered for all these
7 uses, or would they have to actually go and get
8 those --

9 DR. HOWE: The existing radiation
10 oncologists that have the authorization to use
11 therapeutic radiopharmaceuticals are grandfathered.
12 We're talking about the future radiation oncologists.

13 MEMBER DIAMOND: Right. That's what I
14 wanted to be clear upon.

15 DR. HOLAHAN: May I say something? This
16 is Patricia Holahan.

17 CHAIRMAN MALMUD: Patricia.

18 DR. HOLAHAN: I'm getting back to Dr.
19 Diamond's question. What you would have to do going
20 through that residency program as you specified, you'd
21 have the unsealed material, but you'd have to verify
22 it through the preceptor, so you'd have to basically
23 submit a preceptor statement only, not do the
24 additional 80 hours.

25 DR. HOWE: The idea is that you probably

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1 had 80 hours, and then you just -- you get the
2 preceptor to say that you had the 80 hours, and that
3 you have the three cases in the type of material used,
4 because there are two different categories there.

5 MEMBER DIAMOND: I understand.

6 CHAIRMAN MALMUD: Are there any other
7 questions on this point for Dr. Howe before -- I think
8 we interrupted your presentation.

9 DR. HOWE: I think I was very close to the
10 end, and there was probably -- let me see. Here's the
11 radiation oncology for 1000, and I've already said
12 that was 490 and 940. And the next was the background
13 which you just gave for the regulations as they exist
14 right now, so I think --

15 CHAIRMAN MALMUD: I believe there was one
16 more question.

17 MEMBER BAILEY: Yes. Presumably, you
18 would continue the practice if they have been named
19 for that study on any license, and they have
20 essentially demonstrated that they are qualified to do
21 it. For example, right now we are -- several states
22 are probably not following exactly what NRC has for
23 the necessary training and experience, and if they
24 were say on a California license, and they moved to an
25 NRC state, would they still be eligible? Would they

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1 have to go back and prove that they're capable of
2 doing it after they've been doing it for three, four,
3 or five years?

4 DR. HOWE: With the exception of a few
5 places where there's probably oversight, I think in
6 most cases we say or equivalent agreement state. We
7 haven't hit that yet, but I think we would.

8 MEMBER BAILEY: Okay. And the other part
9 is that when you talk about the additional training,
10 you're talking about radiation safety training only.
11 Correct?

12 DR. HOWE: Yes, because if you look at the
13 items that are listed, they are radiation safety
14 items.

15 MEMBER BAILEY: And not --

16 DR. HOWE: But you will see because it's
17 therapy, there are clinical cases because the clinical
18 cases have to cover radiation safety topics because
19 when the new Part 35 was being developed, there was a
20 recognition for therapy, you had to have a minimum
21 clinical experience. That was part of the overall
22 radiation safety for the patient, user, the workers.

23 CHAIRMAN MALMUD: Dr. Williamson.

24 MEMBER WILLIAMSON: This issue of the
25 relationship of -- or the issue of safety only versus

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1 safety plus clinical for 300 has been raised now many
2 times over the last few meetings. I think it would be
3 worthwhile to dig out the Statements of Consideration
4 for the current regulation and determine whether
5 ACMUI's memory is correct. But I know that the
6 consensus was, when we were debating the basis of the
7 current regulation, that a certain amount of clinical
8 experience and expertise, not just safety, is
9 essential to promote public health and safety for
10 35.300 modality.

11 DR. HOWE: That's how I --

12 MEMBER WILLIAMSON: And below that, the
13 consensus was reached that it could be strictly
14 defined in terms of technical safety issues, but at
15 300 and above, clinical expertise was considered to be
16 an important component.

17 CHAIRMAN MALMUD: Dr. Nag.

18 MEMBER NAG: Yes, I would like to put this
19 off until I have made my presentation, because I'm
20 going to be asking and addressing, perhaps more than
21 addressing, asking some of these things.

22 CHAIRMAN MALMUD: Thank you. If I may --

23 MEMBER DIAMOND: Excuse me. I just have
24 one more quick question. What about nuclear medicine
25 residents who are at institutions where although they

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1 have the 700 hours of laboratory and classroom
2 experience, may not have delivered or may not have
3 been proctored on three cases, for example, at Wash U
4 where the nuclear medicine residents may not have had
5 any experience. Do they also have a mechanism through
6 the alternate pathway getting AU status?

7 DR. HOWE: Yes. One of the things that
8 the working group was tasked with doing was to
9 separate out the clinical experience from the boards.
10 That was part of your question, that these folks now
11 have -- meet the qualifications to sit for the boards.
12 Well, part of what the working group did was to split
13 out the clinical experience from the board
14 certification. And so you have this route, board with
15 three cases, alternate pathway with three cases. And
16 it may be that you come in and are an authorized user
17 for certain isotopes and certain therapies because you
18 don't have the case experience. And then later new
19 isotopes come up and you get the case experience in
20 those. You come back in and ask for increase in your
21 authorization, and it's granted because you have the
22 additional training and experience that's gained later
23 on. It's an ongoing evolving type of training and
24 experience.

25 CHAIRMAN MALMUD: Does that answer your

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1 question, Dr. Diamond?

2 MEMBER DIAMOND: It does.

3 CHAIRMAN MALMUD: Thank you. Dr. Howe,
4 you mentioned one thing earlier that I picked up but
5 didn't ask you about. You mentioned vendor training.

6 DR. HOWE: Yes.

7 CHAIRMAN MALMUD: Would you care to
8 elaborate about that at all, or shall I ask you a
9 specific question about the vendor training?

10 DR. HOWE: We normally assume that the
11 vendor knows more about their device or drug than
12 anyone else, at least in the early stages until it can
13 get into the routine training, residency programs or
14 other medical practice, so we generally look for that
15 vendor training as an important concept.

16 CHAIRMAN MALMUD: The vendor training
17 traditionally has been clinically oriented. I would
18 assume that the vendor training for an issue such as
19 radio immuno therapy for board certified physicians
20 who have not done it previously or for microsphere
21 therapy for physicians who have not done it
22 previously, should include some radiation protection
23 and radiation safety issues and dosimetry issues as
24 part of the vendor training, which is really the
25 concern of the NRC, rather than the clinical training,

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1 which we assume was not a direct concern of our's. I
2 would hope that the vendors are aware that this is
3 what they should be providing in the course of their
4 educational process for those who are new to either of
5 these two therapies, regardless of the specialty, the
6 board certification that the physician may have by way
7 of background.

8 DR. HOWE: We don't have as much
9 interaction with say the monoclonal antibodies because
10 they're currently under 300, and so we would not be
11 providing additional guidance on vendor training. We
12 hope that the community will get the training it needs
13 on these new products. But for the 1000 uses, we
14 generally work pretty closely with the manufacturers
15 in understanding their product, developing -- we
16 develop the guidance and we stay in communication with
17 them, and they many times will develop their training
18 to cover the areas that we are specifically addressing
19 in the guidance, so they do address radiation safety
20 issues, in addition to the clinical.

21 CHAIRMAN MALMUD: Thank you. I saw
22 another hand. Dr. Eggli.

23 MEMBER EGGLI: In relationship to the
24 vendor training, how does one document that experience
25 since most of these vendors are not going to be

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1 authorized users and can't officially preceptor that
2 activity.

3 DR. HOWE: I think the working group for
4 developing the new rule has provided some more global
5 language that says for some of these new modalities
6 they have vendor training, or they can obtain training
7 under the supervision of an authorized user, organized
8 microphysicist, or whoever would be appropriate. And
9 the implication there is that your preceptor is a
10 verifier, not necessarily a provider. And that the
11 vendor -- what it says you may meet these by getting
12 vendor training or under the supervision of someone.
13 The vendor training has no specificity on who provides
14 it. Roger Broseus.

15 DR. BROSEUS: Dr. Malmud, may I be
16 recognized?

17 CHAIRMAN MALMUD: Yes.

18 DR. BROSEUS: Roger Broseus. You raised
19 this issue at a previous meeting, and the way the
20 staff is approaching this in the draft final rule is
21 to accept the recommended worded of the ACMUI and
22 include in the definition of a preceptor in 35.2 a
23 person who verifies training and experience, which
24 captures -- so that makes it so that the person who is
25 precepting can verify that a person -- that a

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1 candidate as AU has the training even though that
2 person didn't personally deliver the training, and it
3 would encompass the vendor training.

4 CHAIRMAN MALMUD: Thank you, Dr. Broseus.
5 This is not meant to generate a response, but it's
6 simply a thought that occurred to me during this
7 discussion; and that is that given the availability
8 now of interactive self-education with documentation
9 of having completed an exam regarding a course on a
10 CD, it would probably be wise for vendors to provide
11 such a course, which is inclusive of both the clinical
12 and physics aspects of their therapies so that there
13 could be permanent documentation that this was, in
14 fact, learned by the new practitioner, or the
15 practitioner of this new therapy. That wasn't meant
16 to generate a response from you, because it's just out
17 of the blue. But certainly, it could be the form of
18 documentation that seems to be missing from the vendor
19 educational process.

20 MEMBER DIAMOND: One last thing. Is the
21 NRC aware that there's a whole new class of targeted
22 therapy that is around the horizon which is not
23 technically considered radio immuno therapy? For
24 example, this week at our institution, we are going to
25 be starting a trial for brain tumor patients, which

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1 involves a Scorpion venom chelated to I-131. Now in
2 radio immuno therapy you have a cancer cell with an
3 antigen, and you have a lauding which is an antibody
4 chelated to a radioisotope. In this particular new
5 class of targeted therapy, it's actually a protein
6 sequence that's being recognized, so it's not radio
7 immuno therapy, it's targeted radiotherapy, it's
8 targeted unsealed radiotherapy, but it's not radio
9 immuno therapy. This may be a situation, thus, that
10 the technology is advancing more rapidly than the
11 regulatory space.

12 DR. HOWE: But I would say that if you go
13 back and look at what you're proposing in your
14 clinical trials, and you look at our regulatory
15 framework for 300 use, you may find that our
16 regulatory framework for 300 use fits the radiation
17 safety of your new product. In other words, there's
18 nothing magical about radio immuno therapy. It could
19 have some other name, it could be something slightly
20 different, but if it is covered in our regulatory
21 framework by 300 and the general requirements that go
22 with 300, therapy of unsealed materials, then it may
23 be new to you, but we may not have --

24 MEMBER DIAMOND: But it all gets back to
25 how the regulations are written. If in the language

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1 of the regulation it has that immuno --

2 DR. HOWE: Our regulations don't say
3 immuno. They just say unsealed byproduct material
4 requiring a written directive. And actually, your
5 drug will come under - when you go under 390, you've
6 got I-131 less than value, I-131 greater than a value,
7 and then you've got the other routes of administration
8 and a very global description of what those isotopes
9 are. I'm going to guess it's going to come under that
10 last two groups, and they will be already covered by
11 a regulatory frame.

12 And that was what I was trying to say in
13 the beginning; it may new to you, it may be new to
14 medicine, but we may already have an existing
15 regulatory frame that it fits in, and we don't have to
16 develop any new guidance for it. The structure is
17 probably already there, just from your description.
18 I mean, its medical implications and its practice of
19 medicine issues are brand new, but from our particular
20 radiation safety regulatory framework, it may already
21 be covered.

22 CHAIRMAN MALMUD: Dr. Eggli, did you wish
23 to make a comment?

24 MEMBER EGGLI: No. I think I'm inclined to
25 agree that it sounds like it would be a Part 300 use,

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1 as described.

2 CHAIRMAN MALMUD: Ralph.

3 MEMBER LIETO: That's what I wanted to get
4 to earlier. When Dr. Eggli made an earlier point
5 about P-32 and being a better analogy for the
6 microspheres, we have had a structure dealing with
7 microspheres in nuclear medicine that goes back
8 decades. Okay. It was in the diagnostic
9 applications, but it's been there. I guess, to me,
10 the big problem here has been with the microspheres
11 being classified as a device, and that gets back to
12 the FDA process, which I think maybe we might need
13 some clarification there. But just as you said, if we
14 look at just the radiation safety implications, and
15 the fact that you've already said that these are
16 sealed sources but are exempt or are not going to have
17 to meet the leak testing requirements, then I think
18 you can make a very, very strong case that the
19 microspheres are more accurately, from a radiation
20 safety consideration, is better handled under the 390.
21 And I think that we need to consider that and not just
22 accept the 490 period, and just they're exempt from
23 the leak testing requirements, because if you look at
24 the 400 requirements, if you take out all these leak
25 testing requirements, the precaution -- they're not

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1 any different than the 300s. So I would go back and
2 say that the microspheres, that you can make a very
3 strong case again for them being classified under the
4 300 applications.

5 DR. HOWE: I think Dr. Nag would like to
6 give his presentation.

7 CHAIRMAN MALMUD: Have you completed your
8 presentation, Dr. Howe?

9 DR. HOWE: I have completed my
10 presentation.

11 MEMBER LIETO: Let me clarify on the
12 device/drug issue. FDA has some new laws regarding
13 combination products, and the issue of Yttrium-90 I
14 think right now is a device, but I think the safety
15 issues -- right now, this is where we're at, but I
16 think as more therapeutics get developed, I think
17 you're going to see other issues come to the table.
18 So I think you may want to maintain some flexibility,
19 and in some ways Yttrium-90, it's got a dual
20 characteristic. You can't say it's a device --

21 MEMBER DIAMOND: And also in FDA's
22 defense, it was the manufacturer that made the
23 conscious decision to go through the device pathway,
24 not the drug pathway. That was their decision.

25 MEMBER LIETO: Correct.

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1 DR. HOWE: But it's also -- the way the
2 Yttrium is put into the matrix, it has no
3 pharmacological activity. The Yttrium is sealed and
4 contained in the matrix. It doesn't leech out and the
5 microspheres don't go to where they're going to
6 because of pharmacological activity, where your
7 Scorpion proteins do go to a set location because the
8 receptor concept and your monoclonal antibodies go to
9 a receptor because of their interaction, their
10 pharmacological activity. That's the major basis for
11 the drugs to the devices is in a pharmacological --

12 MEMBER SULEIMAN: Well, you've got to be
13 careful. I think the science may not be - somebody
14 said it - I think the regulatory bounds may be behind
15 the science, and I think from what I've see recently,
16 the science isn't that definitive either. We have a
17 lot of people making all sorts of claims. You're
18 seeing new nanotechnologies where as the particles get
19 smaller and smaller, you really cannot say it's a
20 physical object or how the mechanisms are drug
21 related, or biologics are considered a drug. We have
22 that debate going on within the agency, so I think
23 keeping an open mind, and I think I can promise you
24 that this issue is probably not going to rest here.

25 CHAIRMAN MALMUD: Thank you, Dr. Suleiman.

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1 Dr. Eggli.

2 MEMBER EGGLI: With that analogy,
3 Sulfurcholate administered intra-arterially is a
4 device because it is delivered purely by its flow
5 properties. It is biologically inert, and it in fact
6 is the material used for the dosimetry for Yttrium-90
7 microspheres. So the distinctions are very blurred,
8 and again I guess Ralph and I are sort of reinforcing
9 each other, but there is huge cross-over here. And
10 again, I think the P-32 colloid is a very model in the
11 300 series therapies to effectively describe what
12 these microspheres do. And I think it may be
13 appropriate to look at them from two frames of
14 reference, eliminating the inconsistent portions of
15 each part since, in fact, these microspheres do leak.

16 CHAIRMAN MALMUD: Thank you for your
17 observations, Dr. Eggli. And Dr. Howe, may we thank
18 you once again. You find yourself at the crossroads
19 of rapidly advancing science and regulations, and are
20 always a source of great stimulation to this
21 committee. We thank you for the depth of your
22 knowledge, and for your patience, as well. Thank you.
23 Now Dr. Nag.

24 MEMBER NAG: Thank you very much. What I
25 wanted to do was to give some brief background, some

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1 of my thoughts, not only on the Yttrium-90, but some
2 of the new things that are either there or on the
3 horizon, and what the problems it will create and so
4 on.

5 Now the Yttrium-90, we have been talking
6 about that, but some of us may or may not know some of
7 the details of how it goes on. And I think a little
8 of that knowledge is required to understand how we
9 should regulate that, because the Yttrium-90
10 microsphere, tiny microspheres that are suspended in
11 a solution, and that are injected into the liver via
12 the hepatic artery, so interventional radiologists
13 will do an angiogram, and then we will inject the
14 microsphere into the hepatic artery. And Yttrium-90,
15 most of you know, is a high energy emitter with a very
16 short range in the tissue. And because of the short
17 half-life, most of the radiation is denigrated in
18 about 10 or 11 days.

19 There are two different kinds. One is the
20 SIR-Sphere by the Sirtex Company. The other is the
21 Therasphere by MDS. The two have different properties
22 and, therefore, will be important in the regulations,
23 because although both are Yttrium-90, they do have
24 entirely different properties.

25 The two that we are talking about is the

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1 glass microspheres by Therasphere, used mainly for
2 hepatocellular carcinoma. The glass microspheres are
3 somewhat heavier. They tend to settle down, and not
4 go as much forward. The resin microspheres are
5 smaller particles and they tend to be more free-
6 floating and, therefore, they tend to go forward, and
7 they are used more in the colo-rectal ones.

8 The SIR-spheres, which I'm more involved
9 with and they are FDA approved, they are kept in a
10 vial of three gigabecquerels, so they will always ship
11 you three gigabecquerels and you decide how much of
12 that you would use. Raising about 20 to 60 microns,
13 and they're about 40 to 80 million resins. And the
14 average number that we implant is about two-thirds of
15 that in most cases.

16 Now what we do, we are infusing that into
17 the hepatic artery so that the catheter is placed into
18 the hepatic artery, selectively if possible either to
19 that lobe and, therefore, we are injecting into the
20 entire lobe, or sometimes super-selectively into a
21 part of the lobe. Usually, we are not infusing the
22 whole liver at the time. We are usually doing one
23 lobe at a time. And, therefore, the microsphere will
24 go into the vessel and then they are stuck in the
25 smaller vessel. Once the vessel has about 25 to 75

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1 microns, then the sphere will then embolize.
2 Basically, you have two functions. One is the
3 embolization function where the blood flow is dark,
4 and then it is also radiating at the same time, so you
5 have to know about this combined embolization effect
6 and the radiation effect, because as you are
7 embolizing, you are stopping the blood vessel, and
8 then the microsphere cannot go any further, so you
9 have a harder time injecting all the microsphere you
10 want at some point. So as you can see, the liver
11 vasculature, they become very small. And the smaller
12 vessel will now become totally embolized and no
13 further particle will go into it.

14 So the technical part of injection is
15 somewhat simpler because you just have stopper you're
16 injecting. At one time you're injecting the contrast
17 to see where the flow is going. You are then
18 injecting the microsphere in water to push the
19 microsphere to the place you want, and then you inject
20 more water to separate it from any contrast material.
21 Then you inject more contrast where you going. So the
22 technical part of the injection is reasonably simple
23 but the thing is when you -- how much do you push,
24 when do you stop, and then you have the radiation
25 safety considerations that we'll talk about; which is,

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1 what happens if these particles leak out or if there
2 is a leakage or spillage? So you're injecting it in
3 pulses each time, and when the microspheres are
4 denigrated, you're having embolism of the vessel so no
5 further particle will go in. And, therefore, you're
6 going to have stasis. So let's say at the beginning,
7 we decide to do two gigabecquerels, but if you're
8 having stasis after doing half of it, you have to
9 stop, or you cannot really complete your therapy, so
10 then you can modify and say we now have stasis. We
11 can't give any more.

12 The sum of the radiation safety
13 considerations are that if there's an encapsulated
14 isotope, although they are very, very tiny, they are
15 encapsulated. But functionally, they function like a
16 suspended liquid, so it's more like an unsealed source
17 in that respect that you have commented upon. But the
18 radiation exposure itself is minimal if it is
19 contained. But if it is spilled, then you have the
20 problem of containing that radiation spillage. So,
21 therefore, stasis is an end-point, and more often from
22 what I have done, I have had to end because of the
23 stasis, rather than because I have given the entire
24 two or three gigabecquerels that I wanted to. So we
25 have to have the stasis built into the directive. So

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1 these are some of my thoughts on this.

2 The vendors do give you training. The
3 training includes both radiation safety aspect, and
4 more of it is how to inject and what to do in case of
5 a spillage. That's the major training that we do
6 have. The major consideration I think you need to do
7 is not just the technical aspect of how to inject, but
8 who do you inject, how do you select the patient for
9 that? And those part of the training need to be built
10 into anybody who is going to do Yttrium microsphere
11 therapy; although I realize the medical training part
12 is not an NRC issue, but the safety -- because you can
13 just inject the 3 millicurie or 3 gigabecquerel and
14 not know what's going to happen to the liver. The
15 liver might liquify if you're in excess. Yes, go
16 ahead.

17 CHAIRMAN MALMUD: Dr. Nag, how is stasis
18 determined?

19 MEMBER NAG: When you are injecting, you
20 look for, number one, if you're having difficulty
21 pushing, that's one indication that you may be
22 achieving stasis, but the formal way to see it is you
23 then inject some contrast and you see whether the
24 contrast is flowing forward or if the contrast is
25 having a backflow, or the contrast is not going at

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1 all.

2 CHAIRMAN MALMUD: In practical terms, is
3 this done an interventional radiologist, or by a
4 radiation oncologist?

5 MEMBER NAG: It is done by a radiation
6 oncologist in my place. I know in some other places
7 it's done by either by the interventional radiologist
8 or in some places by nuclear medicine too. I'm not
9 sure --

10 MEMBER DIAMOND: Well, actually, it's the
11 radiation oncologist who's been the AU.

12 MEMBER NAG: Yes.

13 MEMBER DIAMOND: I mean, the catherization
14 has been done by interventional radiologists.

15 MEMBER NAG: Yes. The catheter will be
16 placed by the interventional radiologist. Once he
17 puts the catheter into the site I want, whether it be
18 the left or the right hepatic artery, or the main
19 hepatic artery, we decide and we tell them where we
20 want it, then we take over and we start injecting the
21 radioactive material.

22 MEMBER DIAMOND: And if I may, the issue
23 of stasis is therefore determined not by the
24 interventional radiologist, but by either the
25 radiation oncologist or nuclear physician who is doing

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1 the administration?

2 MEMBER NAG: Whoever is doing the
3 injection. I mean, if it's done by the radiation
4 oncologist, we do it. Sometimes we may ask the help
5 of the interventional radiologist, do you think it's
6 going forward, or do you think we can push any more?

7 MEMBER DIAMOND: It's actually quite a
8 little art with back and forth as you do these,
9 particularly with these super-selective cases. You
10 can actually get a feel on these catheters, and get a
11 sense of the resistance, and almost get a -- just like
12 an experienced interventional cardiologist can kind of
13 feel the guiding catheter.

14 CHAIRMAN MALMUD: Perhaps I'm not being
15 specific enough, and I'll try and be more specific.
16 Is the -- I understand that the placement of the
17 catheter is done by an interventional radiologist.

18 MEMBER NAG: Yes.

19 CHAIRMAN MALMUD: That's that person's
20 expertise. Is the injection done in the
21 interventional room, or is it done in a radiotherapy
22 room?

23 MEMBER NAG: No, it has to be done in the
24 same place where the interventional catheter is in
25 place, because you don't want the catheter to move.

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1 You have the fluoroscopy, so it is done in the
2 interventional radiology suite.

3 CHAIRMAN MALMUD: So this is a conjoint
4 effort of interventional radiology and a specialist in
5 radioisotopes or radiation oncology.

6 MEMBER NAG: Right.

7 CHAIRMAN MALMUD: Thank you.

8 MEMBER NAG: You had a question.

9 DR. HOWE: Could I just clarify?

10 CHAIRMAN MALMUD: Please do. Dr. Howe.

11 DR. HOWE: I'd just like to clarify that
12 we recognize that stasis was probably the best end-
13 point, and so when we modified the guidance for the
14 Yttrium-90 microspheres about a year ago, and we added
15 stasis as an option for the authorized user to write
16 into the written directive in advance of providing the
17 material, so that it would be clear that if they
18 stopped the injection based on stasis, we weren't
19 looking at medical events. This was the best end-
20 point, so we have included that in our guidance for
21 the written directive.

22 MEMBER NAG: Yes.

23 CHAIRMAN MALMUD: Thank you, Dr. Howe.
24 Dr. Williamson.

25 MEMBER WILLIAMSON: Yes. Are the SIR-

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1 spheres regulated also as a sealed source?

2 MEMBER NAG: Yes.

3 CHAIRMAN MALMUD: The answer to Dr.
4 Williamson's question was yes, from Dr. Howe.

5 MEMBER NAG: Now I'm not going to say very
6 much about the antibody therapy since Donna covered
7 that very well. I had intended to, but I will skip
8 over those things. I want to introduce something
9 called pulse dose rate. Many of you may be aware,
10 some of you may not. The reason why I want to
11 introduce this is it's a different method that has
12 some regulation problem. I want to give a brief
13 overview as to why it is being introduced, and it is
14 a remote afterloader.

15 Now in a way, it is very similar to the
16 HDR afterloader. The difference being that in the HDR
17 you have a 10 curie source. Here you have a one curie
18 source. And what the pulse dose does is instead of
19 giving radiation at the high dose rate continuously
20 for 10, 15 minutes, it brings more pulse dose
21 radiation for a few minutes every hour. The
22 traditional one is every hour. There have been other
23 modified versions of doing it for three hours, then
24 off for a few hours and so on, but the traditional one
25 is giving pulses of radiation usually at about 50 to

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1 100 Centigrade in about ten minutes within that first
2 part of the hour. And then, the rest of the 50 minutes
3 there's no radiation, so that allows personnel to get
4 in, look at the patient, do all the nursing care
5 without any radiation exposure hazard. And then you
6 can vary the length of the pulse and the time and so
7 on, so that the -- many of the characteristics are
8 like HDR, many of the advantages of HDR, but because
9 you are giving a small dose per hour, usually about 50
10 Centigrade, the radiobiology is more like a low dose
11 rate radiotherapy. And the source itself is a lower
12 activity, usually about 0.5 to 1 curie, so if you are
13 doing it, the low dose rate is continuous at the low
14 dose rate over a few days, two to five days. High
15 dose rate, you're giving very high doses for the short
16 period of time, usually once a day or twice a day.
17 But in pulse dose rate you are giving a small amount
18 of dose, impulsing every hour or so over a period of
19 a few days. So these are the basic differences
20 between the two.

21 What are some of the advantages? Why do
22 you want to do it? Because you have only one Iridium
23 source. You don't have to have multiple Iridium
24 source that you have to take care of. The major thing
25 is that you are having minimal risk of exposure to the

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1 personnel. You are eliminating the radiation exposure
2 hazard, and at the same time, you are having the
3 radiobiological advantage of low dose rate
4 brachytherapy.

5 Some of the problems that you are going to
6 need a few days to deliver the radiation and,
7 therefore, the patient has to be in the hospital for
8 those days; and, therefore, you have some of the
9 problems of prolonged bedrest and so on. There's the
10 potential movement of the basin during those two or
11 three days, and there is the potential that by the
12 patient moving, you may kink the catheter or the
13 applicator and, therefore, the source may have a hard
14 time either going in or coming back.

15 There are some radiobiological issues - is
16 50 Centigrade delivered in a few minutes every hour
17 the same as a continuous 50 Centigrade power. Some of
18 those things may have to be continued to be explored,
19 but the radiation safety consideration of that - the
20 source activity is much lower than HDR, about one-
21 tenth. And, therefore, there is less shielding
22 requirement. Now the question is for the HDR do you
23 need to have the physical plantings of an authorized
24 user and physicist during the whole therapy. Here,
25 the therapy is for a few minutes every hour, which

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1 means from a practical standpoint, you would need a
2 physicist and/or an authorized user in the patient's
3 room continuously for two or three days. That's not
4 really very practical, and some of these
5 considerations will have to be thought about. The
6 reason why the part dose rate concept has come up, it
7 has been around for quite a number of years, but
8 because of the radiation safety consideration, it has
9 not come up very much in U.S., but it is gaining a lot
10 of importance in Europe. And, therefore, many people
11 in the U.S. are thinking of taking it back again,
12 especially those who are not very comfortable using
13 HDR because of the radiobiology, and are comfortable
14 with LDR, but at the same time, they like the
15 radiation -- elimination of radiation hazard that the
16 HDR produces.

17 CHAIRMAN MALMUD: Dr. Williamson.

18 MEMBER WILLIAMSON: Well, as I recall, a
19 great effort was made to craft 35.600 to make it
20 practical to license pulsed dose rate. It is
21 mentioned specifically in 35.600, and not all the HDR
22 regulations apply exactly to it. I don't know that
23 anybody has ever submitted an amendment for it to
24 really test how well that regulation works, but an
25 effort was made to basically make it practical to use.

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1 MEMBER NAG: The reason I brought this up
2 is so that the NRC is aware - I mean, once you are
3 getting a floodgate of all the applications of people
4 who are planning PDR you want to be prepared for it,
5 so I wanted to give you a head's up. I'm not saying
6 we have any solution. I'm asking to be prepared for
7 it.

8 CHAIRMAN MALMUD: Thank you for bringing
9 the matter to our attention and educating us,
10 especially those of us who are not familiar with the
11 issue. Are there any other comments to Dr. Nag
12 regarding this presentation?

13 MEMBER NAG: Now I want to go on to the
14 next one, which is again - we are getting a lot of
15 these combos. Now we are going to be talking about I-
16 125 afterload, and this is something that has been
17 presented here before. We had asked it to be at this
18 meeting because of some of the regulation issues. The
19 I-125 afterloader basically is very similar to the way
20 we do our manual prostate brachytherapy, in that it is
21 I-125 seeds that are implanted into the patient. And
22 what I want to do is show how it is somewhat different
23 from the manual prostate brachytherapy. But because
24 it is termed a remote afterloader, many of the
25 regulatory issues of the remote afterloader for HDR is

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1 sort of mixed with this, so I would like to present it
2 so you have an idea what it is.

3 Basically, you are having all the seeds
4 now in a sterile cartridge that is shielded, so now
5 you don't have the issue of handling a new seed, so
6 the seeds are in one cartridge that cannot be opened.
7 It's a fixed cartridge, so to some extent there's some
8 safety in that, that the seeds cannot get loose. You
9 cannot have seeds dropped on the floor and so on.

10 You have one cartridge that will have all
11 seeds. You have another cartridge that has all
12 spacers. So in prostate brachytherapy, what you do is
13 you put one seed, one spacer, one seed, one spacer.
14 This will allow you to make your seed spacer assembly
15 in the OR, so if in the OR you do the prostate
16 ultrasound and you plan that you want seed-spacer,
17 spacer-seed, seed-spacer, or any combination, you can
18 make it up in the OR in real time. And then the
19 afterloader has its calibration the capacity to
20 recognize whether what you planned is what is in that
21 assembly.

22 For example, although it will not
23 calibrate the source directly, it will tell you
24 whether you're having a source at this position, or a
25 spacer. So if you had source-spacer, source-spacer,

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1 and the one that is going in is to confirm that this
2 was the assembly as you had planned. So there is some
3 amount of verification built into it.

4 The other difference is that normally at
5 this point, I would manually push the radioactive seed
6 spacer in manually. Here the afterloader pushes that
7 grain into the basin and force the needle out. So,
8 therefore, it is a remote afterloader, but the
9 activity of the seeds are extremely low and,
10 therefore, it doesn't require any shielding. So the
11 radiation precautions are very much less compared to
12 HDR; although, because it's a remote afterloader, many
13 of the things that are required for HDR are placed
14 into a I-125 afterloader. And I think that will
15 become burdensome, and will prevent or it will
16 discourage some of the users from using it because
17 they have to meet a lot of the regulations that
18 probably are not totally appropriate for this.

19 It does have computer verification of seed
20 basin. You do want to know whether what you had
21 planned is what is going in. You do want to be able
22 to confirm that the needle is going to the place you
23 wanted it to go, and the afterloader does that. The
24 other difference is that in a regular remote
25 afterloader, you want to confirm that the source that

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1 went into the patient comes back into the remote
2 afterloader. Here, the source going into the
3 afterloader, but does not come back from the patient.
4 It's permanently implanted in the patient. So these
5 are, from my standpoint, some of the safety
6 considerations. We may need some discussion as to the
7 way the regulations are written at the moment in an
8 attempt place an over-burden on the licensee, because
9 many of them may not apply.

10 CHAIRMAN MALMUD: Dr. Williamson.

11 MEMBER WILLIAMSON: I think Dr. Nag is
12 exactly right, that this is low dose rate permanent
13 seed implant, and the regulations should be written,
14 additional regulatory burdens should be very
15 minimalist in the sense of only addressing the unique
16 technical characteristics of this machine, and not
17 impose any additional regulatory burdens beyond those
18 in 35.400 for permanent seed implants. There's no
19 need for the prescription to be any different.
20 There's no need for a facility diagram, because this
21 is not a high dose. You don't require that for
22 permanent seed implant, so I do think that at least
23 the second iteration of the guidance that I reviewed
24 seemed to me to be too -- overly influenced by the
25 existing HDR remote afterloader regulatory framework.

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1 CHAIRMAN MALMUD: Mr. Lieto.

2 MEMBER LIETO: Yes. I guess I have -- I
3 agree with Jeff and Dr. Nag on this, but I guess I
4 have a question regarding the word "remote". I'm
5 always picturing remote as that you have to be outside
6 the room when the sources are being placed into the
7 patient, and then retracted.

8 MEMBER NAG: In this case, the doctor is
9 in the room, and basically you are standing by the
10 machine. You are not outside the room. But the word
11 "remote" is there because it is not the doctor who is
12 pushing that source. It's the machine that is pushing
13 the source, so that's where the remote comes in. But
14 I think that it is unfortunate because because of the
15 word "remote" all the remote HDR regulations comes
16 into play, when really there is no need.

17 CHAIRMAN MALMUD: So if I may, it seems
18 that Dr. Williamson is saying that some of the
19 existing regulations may be excessive for the
20 application of this particular therapy using this
21 form.

22 MEMBER WILLIAMSON: It's actually
23 guidance. There are no regulations for it.

24 CHAIRMAN MALMUD: The guidance may be
25 excessive regarding this form of therapy, and Mr.

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1 Lieto is saying that the use of the term "remote"
2 means something else in this case, that the word means
3 something else.

4 MEMBER NAG: Right.

5 CHAIRMAN MALMUD: And you wish to bring
6 that to the attention of NRC.

7 MEMBER LIETO: Right. I just don't think
8 we should address this device as a remote afterloader.

9 CHAIRMAN MALMUD: That in this case the
10 word means something else, or its application means
11 something else.

12 MEMBER LIETO: Yes.

13 MEMBER WILLIAMSON: You could make a case
14 that it could be in 35.400. It's just the --

15 MEMBER NAG: I think from a regulation
16 standpoint --

17 MEMBER WILLIAMSON: I mean, that would
18 make most sense to start with 400 as the foundation.
19 And I think you can argue it both ways. It is a more
20 complex device. It is replacing a human activity by
21 a mechanized robotic device. There are error pathways
22 that have to be looked at from a clinical physicist
23 point of view. There certainly needs to be a far more
24 sophisticated quality assurance program to ensure that
25 the device works properly. And I guess the issue

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1 would be whether one would be performance-based or
2 prescriptive with regard to that. But there are many
3 things in the 600 regulation which at least in the
4 version that I saw at the end of June, which continued
5 to be copied out of 600, which seemed to me to be
6 inappropriate for guidance for using this device.

7 MEMBER NAG: This technology is the
8 marriage between something in the 400 category and
9 something in the 600 category. And because it was a
10 remote afterloader, the primary thing came from the
11 600 from the regulation standpoint, came from 600,
12 eliminating a few things from 600, so that it becomes
13 compatible with 400. From a physician standpoint, I
14 would say that this is more of a 400, and you may want
15 to bring a couple of things in from 600 just to meet
16 the afterloading capabilities, so that makes a big
17 difference in the regulations.

18 CHAIRMAN MALMUD: Dr. Nag, if I may bring
19 the comments of the three of you together. Are you,
20 and Dr. Williamson, and Mr. Lieto recommending that
21 NRC staff consider this particular type of therapy to
22 be more appropriately classified under 400 than 600?
23 Is that the recommendation that you are making that
24 they consider?

25 MEMBER NAG: Yes, with the extra

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1 precaution that may need to be brought in because it
2 is an afterloader device.

3 MEMBER WILLIAMSON: I would say it's the
4 issue of, it's a 1000 device. Okay. They have made
5 the determination, and we could argue that basis, but
6 I think they have a reasonable case that it's a 1000
7 device. And really, the issue is should the guidance
8 be drawn more from the 400 side or the 1000 side. And
9 I think the three of us are saying that it is
10 essentially a 400 application with the need to borrow
11 a few extra things from 1000 to cover the added
12 technical complexity and error pathways that this
13 device introduces.

14 CHAIRMAN MALMUD: I'm trying to summarize
15 your three comments so that we could make a
16 recommendation for consideration to NRC staff. And I
17 guess the first comment would be that this is a 1000 -
18 is this considered a - this is a 1000 device, and that
19 the parties who have just spoken, which include a
20 member of the Radiation Oncology Medical community, as
21 well as two physicists, would wish NRC staff to
22 consider this as - which it already does, as a 1000
23 device with more of the 400 applications than the 600.
24 Dr. Howe, do you wish to comment?

25 MEMBER NAG: I think Dave might want to

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1 make some --

2 CHAIRMAN MALMUD: I'm sorry. I didn't
3 even notice that you put hand up. I'm sorry.

4 MEMBER DIAMOND: No, I was actually just
5 sneezing. I concur with everything that was just
6 said. That's how you go to an auction and you end up
7 with something very expensive.

8 DR. HOWE: NRC is currently in the process
9 of revising our guidance for this device. And I would
10 say that we're probably somewhere around 80/20 percent
11 on the split between 400 and 600, with the 600 being
12 somewhere between 20 percent. And we have revised it
13 since, Jeff has seen it. WE're working now on format,
14 and if we can get the format issues resolved, then
15 we'll be sending it out. And it is moving closer and
16 closer to the 400 than it was before. It's always
17 been more on the 400 than on the 600. We're just
18 continually moving it more and more towards the 400.

19 CHAIRMAN MALMUD: Do the members of this
20 committee who are knowledgeable in this area agree
21 that this should continue to move more in the 400
22 direction than the 600?

23 MEMBER WILLIAMSON: Yes.

24 CHAIRMAN MALMUD: Is there any dissention
25 from that? So you have pretty much a consensus of the

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1 opinion of the committee to consider as you move
2 forward in your deliberations.

3 MS. WILLIAMS: Pardon me. May I suggest
4 that you make a formal recommendation for the public
5 record, please.

6 CHAIRMAN MALMUD: Is there a formal
7 recommendation that this 1000 device be considered
8 under the 400 regs rather than the 600, as a
9 recommendation from this committee? Is there such a
10 recommendation?

11 MEMBER WILLIAMSON: May I restate it?

12 CHAIRMAN MALMUD: No, there is not. Dr.
13 Nag.

14 MEMBER NAG: I think --

15 CHAIRMAN MALMUD: I'm sorry. You shook
16 your head before. You said restate it, so okay. Dr.
17 Williamson, you want to comment first.

18 MEMBER WILLIAMSON: Okay. Whereas, the
19 seeds electron may be appropriately considered a 1000
20 device, the ACMUI recommends that the NRC build upon
21 the 35.400 regulatory framework, adding only those
22 elements of 600 as absolutely needed.

23 CHAIRMAN MALMUD: That is a motion. Is
24 there a second to that motion?

25 MEMBER NAG: Yes.

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1 CHAIRMAN MALMUD: Is there any further
2 discussion? If not, all those in favor of this
3 recommendation. Any opposed? Any abstentions of
4 those who are knowledgeable in the area? So you have
5 a consensus from this committee for your
6 consideration. Thank you. Dr. Nag, you still have
7 the floor.

8 MEMBER WILLIAMSON: I would also add the
9 recommendation that I think once this goes through,
10 and once another revision is prepared, it might be
11 worthwhile submitting it to the sub-group of us that
12 is interested, and have some expertise in it.

13 CHAIRMAN MALMUD: Dr. Howe, there's an
14 expression of interest from this group to see the
15 working document that you will have completed at such
16 time that you will have had the opportunity to
17 complete your deliberations.

18 DR. HOWE: That's fine with us.

19 CHAIRMAN MALMUD: Dr. Howe agrees.

20 MEMBER NAG: I would like to introduce a
21 new isotope that has recently become FDA approved, and
22 will come into medical practice very soon, if not --
23 I mean, it has been started in a couple of centers.
24 So basically, it's Cesium-131. Most of you have heard
25 about Cesium-137 that is used for GYN use. This is

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1 entirely different. Only the name Cesium is the same,
2 but the isotope properties are entirely different.

3 In many respects, Cesium-131 is somewhat
4 similar to I-125 and Palladium-103. It has low
5 energy, it's a gamma emitter, and it has a short half-
6 life. The difference being that the half-life of
7 Cesium is much shorter than Palladium or Iodine, which
8 means that from a basin standpoint, you can deliver
9 the radiation in a much shorter period of time. The
10 energy of the Cesium is very close to Iodine and
11 higher than Palladium, which means the penetration is
12 more than Palladium. Palladium is very good in terms
13 of short half-life, but in some cases the clinicians
14 felt that there may not be enough penetration. Here
15 you are getting the penetration property of Iodine,
16 and even shorter half-life than Palladium, so you are
17 getting, you need to give a little lower dose, 105.28
18 compared to 125, and the initial dose rate is higher.

19 The advantage of the initial higher dose
20 rate is that if you have a higher dose rate, tumors
21 that are fast growing can be treated with Cesium,
22 which may not be well-treated Iodine. So that's the
23 reason why this isotope was thought about. It had
24 been thought about many, many years ago, but in terms
25 of getting it FDA approved, it has only become

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1 clinically available now.

2 We think that the major use is going to be
3 for permanent prostate implant. However, it could
4 very easily be used for other permanent implants, or
5 as a removable implant in eye plaques, or maybe even
6 in breast cancer therapy.

7 The major problem or the major
8 disadvantage is the because the half-life is so short,
9 it has a very short shelf life, which means that you
10 have to use it on the day it was ordered or maybe at
11 the most you can delay it by a day or two. You cannot
12 keep it in for the next week.

13 In terms of radiation safety
14 considerations, I believe that it's going to be almost
15 the same or very similar to that for permanent Iodine
16 or permanent Palladium implant. The energy is low.
17 The seeds are exactly the same size, and the
18 encapsulations are the same. I believe there should
19 be no difference than Palladium or Iodine. The
20 advantage is that if you are going to start the decay
21 you need to store it for only a much shorter period of
22 time. Other than that, I don't see any major safety
23 consideration, and it should be under the regular 400
24 applications.

25 CHAIRMAN MALMUD: Thank you, Dr. Nag, for

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1 that information.

2 MEMBER NAG: Any comments?

3 CHAIRMAN MALMUD: Any questions or
4 comments to Dr. Nag?

5 DR. Zelac: Question.

6 CHAIRMAN MALMUD: Dr. Zelac.

7 DR. ZELAC: Dr. Nag, I presume that since
8 you brought this to the advisory committee, this is
9 reactor produced material, the Cesium-131?

10 MEMBER NAG: I think it's produced by
11 cyclotron. Jeff, you might have to help me out there.

12 MEMBER WILLIAMSON: I don't know, to be
13 honest. I'm trying to think whether it is. I think
14 it can be done by either. Now which it is -- what the
15 vendor is actually doing, that's a good question.

16 MEMBER NAG: The vendor that's producing
17 it is called Isoray. It's a company I haven't heard
18 of before.

19 MEMBER WILLIAMSON: Yes. The AAPM
20 Subcommittee on photon emitting brachytherapy
21 dosimetry is developing a standard data set, and
22 seeing that it's integrated into the same system of
23 national standards as Iodine and Palladium seeds, so
24 dosimetry-wise, not really a big difference. That's
25 a good question. What do you do about Palladium now?

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1 You do not regulate Palladium.

2 CHAIRMAN MALMUD: Was that a question from
3 you, Dr. Williamson?

4 MEMBER WILLIAMSON: Yes.

5 CHAIRMAN MALMUD: Addressed to Dr. Zelac
6 or Dr. Howe?

7 MEMBER WILLIAMSON: Either.

8 DR. HOWE: As long as all of the
9 Palladium-103 is being produced by accelerators, then
10 we don't regulate it. There has been some talk about
11 manufacturers switching over to reactor-produced, and
12 if that occurs, then we will be back into Palladium.

13 CHAIRMAN MALMUD: Thank you, Dr. Howe.
14 Which really indirectly addresses the answer to Dr.
15 Zelac's inquiry.

16 MEMBER NAG: Yes.

17 DR. ZELAC: Indeed.

18 CHAIRMAN MALMUD: Indeed it does. Thank
19 you.

20 MEMBER NAG: I have then a question back
21 to either of you. If you are having an obvious
22 medical event produced by I-125 seed in the prostate,
23 where let's say the seed did not go to the prostate,
24 went to the rectum or so on, that will come under the
25 NRC purview. And if the same problem was created by

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1 a Palladium seed, you would have no jurisdiction over
2 it, or what would happen to that patient?

3 DR. HOWE: We only have jurisdiction over
4 byproduct material, and so if the same thing happened
5 with a non-byproduct material, like Palladium-103,
6 then it would be some other group, or no group at all,
7 that would have jurisdiction over it. So in the
8 federal facilities, because the states are not
9 involved in federal facilities, then it would be just
10 the federal facility that would have the oversight.
11 It would not be the NRC.

12 CHAIRMAN MALMUD: Yes.

13 MEMBER BAILEY: Typically, the agreement
14 states would report that through the NMED system, do
15 the same sort of investigation they would if it occurs
16 in a state jurisdiction. There's no requirement that
17 they do it, but typically that's -- because quite
18 frankly, we don't keep up with which it is. If it's
19 radioactive material, we treat it that way.

20 CHAIRMAN MALMUD: Dr. Williamson.

21 MEMBER WILLIAMSON: Two short comments.
22 One, I think it would be sort of short-sighted for the
23 NRC to totally ignore this. In fact, I think many of
24 the states will probably pattern their regulatory
25 approach after the one developed by NRC for Iodine-125

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1 implants, so there's a close connection, and it's well
2 to be aware of this.

3 I think an error pathway that exists with
4 this is the short half-life, which is going to place
5 a lot more stress on the skill of the -- it's another
6 constraint on where you place the seeds and how many
7 you place to try to compensate for a one-day shift in
8 the activity, so there's probably a small possibility
9 of there being more variability of the delivery dose
10 relative to the prescribed dose, because the source is
11 so rapidly decaying. But other than that, I think
12 that Dr. Nag is completely right, that the practical
13 clinical and safety problems are nearly the same.

14 CHAIRMAN MALMUD: Any other comments
15 regarding this issue? Dr. Suleiman.

16 MEMBER SULEIMAN: Well, FDA has an adverse
17 event reporting system.

18 CHAIRMAN MALMUD: That's why I looked at
19 you. I was hoping you were going to make a comment.

20 MEMBER NAG: The thing is, there may be no
21 adverse effect on the patient because you can place 50
22 percent of your seed outside the prostate, below the
23 prostate, and so long as you're putting it in a
24 radiosensitive organ like the rectum, you are not
25 going to have any adverse problem. The tumor may not

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1 be cured, but we don't cure 100 percent of tumors, and
2 that way if you have a failure, you are not going to
3 know whether the failure was because the seeds were
4 not totally placed in the prostate, or whether the
5 tumor itself was more resistant.

6 MEMBER SULEIMAN: I think this falls into
7 that gray area of, is this the uncertainty associated
8 with the imprecision of medical practice, or is it a
9 known failure where people should have known better.
10 So yes, I think we're in that gray area, but if it's
11 an adverse event or severe adverse event, there is a
12 responsibility on the facility to report that. But if
13 you feel it's under the medical realm, you don't.

14 CHAIRMAN MALMUD: Thank you for your
15 input, Dr. Suleiman. Thank you, Dr. Nag, very much
16 for a very stimulating and informative presentation.
17 It is now time for us to take a break. May I ask
18 staff what time you would like us to rejoin. Shall we
19 abbreviate lunch to 45 minutes or keep it at an hour?

20 MR. ESSIG: If we could abbreviate it to
21 45 minutes, that would allow us to remain reasonably
22 on schedule.

23 CHAIRMAN MALMUD: Is that agreeable to the
24 committee? Then we will reconvene promptly at 1:30.
25 Thank you.

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1 (Whereupon, the proceedings in the above-
2 entitled matter went off the record at 12:42 p.m. and
3 went back on the record at 1:38 p.m.)

4 MEMBER WILLIAMSON: We will pick up with
5 the agenda, if we may, beginning with the first topic
6 after lunch which is the registration of brachytherapy
7 sources.

8 MR. ESSIG: Dr. Malmud, if I may?

9 CHAIRMAN MALMUD: Please.

10 MR. ESSIG: The listed speaker, Mr. Tim
11 Harris, will not be the speaker. Instead, it will be
12 Dr. John Jankovich who is our team leader for the
13 sealed source and device review team. Originally, we
14 wanted to have him, but he was going to be out of the
15 country and that trip was rescheduled, postponed and
16 so now he's able to be here with us.

17 So Dr. Jankovich will be doing the
18 presentation.

19 CHAIRMAN MALMUD: Thank you, Tom. And
20 thank you, Dr. Jankovich for being with us.

21 DR. JANKOVICH: Thank you. Good
22 afternoon. Can you hear me all right?

23 So I am the team leader for the
24 registrations here at the NRC. But NRC has another
25 function. That is to reorder sealed sources and

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1 devices nationwide, that is what the agreement states
2 approve also. So overall we have in the system four
3 and a half thousand registrations and they are coming
4 from 1,200 vendors. That's the nationwide picture.
5 And we want to narrow it down, focus down on
6 brachytherapy sources, but before we proceed, I'd like
7 to give you a few minutes of over view, what the
8 registration sheet is and what it contains and how it
9 specifies its use. Otherwise, we'll proceed to the
10 next slide.

11 (Slide change.)

12 MEMBER WILLIAMSON: Which handout are we
13 looking at?

14 MS. WASTLER: I'm sorry, there's a tab
15 missing.

16 The header says sealed source and device
17 registration in big letters. It's right off your --
18 let's see -- it's right after Dr. Nag, the tab for Dr.
19 Nag's presentation?

20 MEMBER WILLIAMSON: Thank you.

21 DR. JANKOVICH: The names and words we are
22 using here, registration certificated, the name of the
23 official doctrine. However, in the community, people
24 refer to it as SSD sheet for sheet. SSD stands for
25 sealed source and device and sheet for registration

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1 certificates. So you may hear on the sheet words that
2 means the entire document.

3 And what's the content of this document?
4 It describes the design. It has a section on labeling
5 that identifies features. It specifies the conditions
6 of normal use. Shows further type testing and the
7 classification standards, if that source or device was
8 tested to a standard. That's important because we
9 will be talking about these tests and standards in a
10 short while.

11 Luckily, all the registration certificates
12 issued either by the NRC or the agreement states
13 follow this format, so it's easy to understand, easy
14 to see what it contains.

15 Continuing with the content, you can see
16 that the presence of radiation profiles. This is not
17 radiation that goes to the patient. It is
18 occupational radiation profile around the device. As
19 my second bullet shows here, it is the radiation
20 profile really is for specifying what dose
21 occupational dose the physician, the technician would
22 get during one procedure or during daily procedures
23 and then in storage or handling multi-units and what
24 happens if there is a failure or what is the dose rate
25 when they dispose of a single unit.

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1 In addition, the sheet registration
2 certificate sets limits and other considerations of
3 use. That's the official term. What it means is if
4 there are any restrictions, that's also spelled out,
5 the restrictions for its use.

6 And finally, I want to call your attention
7 to this website, all four and a half thousand
8 registrations are evaluated at the NRC website, the
9 full text of the document.

10 Now let's focus down to brachytherapy
11 sources. I searched the system and I found 22 seed
12 registrations only. Three sheets issued by the NRC
13 and 19 issued by agreement states. That's important
14 for everybody to know. As you see, NRC doesn't have
15 a major role to play. Actually, if you are curious,
16 I can easily list. NRC approval is for Best Medical
17 here in Springfield, Virginia, locally for Kennedy and
18 for Dragsomich, and third is Mills Biopharmaceutical
19 from Oklahoma City. Oklahoma is an agreement state,
20 but they have a few SSD vendors. They don't want to
21 have staff qualified for this purpose. It would be
22 cost efficient for them, so then Oklahoma delegated
23 this function to the NRC. Thus, that's how we got
24 into the picture.

25 I looked at all of these 22 sheets

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1 regarding conditions of normal use because I assume
2 that's your primary interest here today. And luckily,
3 there is a fairly good agreement, how well these
4 sheets description the conditions of use, normal use.
5 And these are the three or four terms I found:
6 permanent or temporary interstitial treatment, used as
7 implant by use of commercially available implant
8 tools. That's all.

9 Of course, the FDA's 510KF rule specifies
10 its medical use. NRC is concerned about radiation
11 safety and agreement states similarly are concerned
12 about radiation safety. So that's how these
13 registration sheets specify the conditions of use.

14 Let's talk about testing, testing of the
15 sources because that defines these conditions of use.
16 The regulations, both agreements state that NRC are
17 fairly simple. The first bullet specifies it. The
18 source must maintain its integrity when subjected to
19 conditions of normal use and likely accident
20 conditions. And those are the two things which the
21 regulations require.

22 We are not specific, not restricted. And
23 what are the normal use conditions in likely
24 accidents? The manufacturers are the ones who specify
25 to us. They submit an application. In the

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1 application, they tell us who the reviewers, the
2 technical staff at the NRC and the agreement states
3 and so that's condition, the extent that these
4 registration sheets permit the use of these sources.

5 MEMBER VETTER: Excuse me?

6 DR. JANKOVICH: Yes.

7 MEMBER VETTER: So when an Iodine-125
8 source is sheared in half by a mic applicator, that's
9 not considered to be a likely accident condition,
10 apparently?

11 DR. JANKOVICH: It depends if the
12 manufacturer presented it to us and then if the
13 reviewer accepted that as a likely scenario.

14 What I want to highlight here is there are
15 22 registrations, reviewed by 22 people all over the
16 country and with our set conditions. The only
17 guideline they have is normal use and likely
18 accidental conditions.

19 And then we come to the end of my
20 presentation and probably your meeting, you will come
21 to the conclusion that I will recommend that we try to
22 look for some uniform approach and that would be my
23 recommendation.

24 Going on where the second bullet says we
25 do require actual testing, engineering analysis is not

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1 acceptable because the source and its containment is
2 so important. If it's a device or something, we can
3 accept engineering analysis. What is the passing
4 criteria? Very simple. It says it must maintain its
5 integrity. And how do we determine that? It means
6 integrity that no radiative material leaks after the
7 tests. So there are accepted testing methods for
8 leaking in the standards or the manufacturer can
9 propose their own method.

10 Now let's talk about some standards. Of
11 course, prototypes or C-sources can be tested to
12 standards. There are two standards in use at the
13 present time. American Standard, the so-called ANSI,
14 43.6, and the International Standard, ISO, 2919.
15 Please remember this ISO number 2919, because that's
16 very relevant to brachytherapy. I will talk about it
17 more later.

18 And then when the regulatory body approves
19 this design, we reference the standard with a
20 classification number, last bullet here, because that
21 is universally acceptable and understood that these
22 were tested to that standard according to these
23 conditions. And I explain it quickly on the following
24 slide.

25 But let's finish here with the other

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1 standards. That is for your information only. There
2 used to be two other standards specific to
3 brachytherapy sources. This one, the 43.6 issued in
4 1977. Then withdrawn in 2004.

5 I am talking here about going back, about
6 the present, active standard. This is 43.6. This was
7 issued in -- the latest revision in 1997. As you
8 know, these standards are living documents and they
9 get revised, updated, periodically. ANSI, the
10 American Standard Institute likes to do it every five
11 years. I'm the delegate to this standard from the NRC
12 and we just finished the latest update this summer and
13 it was sent to ANSI for final publication.

14 I want to show that this standard doesn't
15 address brachytherapy sources even during this latest
16 revision. I can tell you why. The working group
17 brought up the subject and who is on the standard?
18 Regulatory representatives like myself and also the
19 industry and in the working group we didn't have
20 really any manufacturers of brachytherapy seeds, so
21 there was no representative there who could have
22 represented this segment of the medical standard. And
23 for that reason, the brachytherapy sources didn't get
24 included.

25 But let's go the second one, to the ISO

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1 standard, 2919. That was last updated 1999. They had
2 a technical committee had a working session in March
3 in Buenos Aires and I am also the NRC delegate to that
4 committee and the brachytherapy and other sources were
5 not on the agenda, even though my manager, Tom Esse
6 approved my travel, I couldn't go. Well, I missed a
7 good trip.

8 Let's go back seriously. What I want to
9 show you here is that there used to be two other
10 standards. Now the old ones, this one issued in 1977,
11 integrity and test specifications for brachytherapy
12 sources. That is how to design them and test them.
13 But this was withdrawn in 1995. And there was another
14 test, the leak testing for brachytherapy sources and
15 was withdrawn in 1984. That was to show how you check
16 the prototype test results. Is there a leak or not?
17 These two tests are here for reference.

18 Now let's look at what the present only
19 active standard contains. That is the international
20 standard. In yellow, I highlighted for you. This is
21 an important table from the standard because it
22 specifies the usage of all the sources and that what
23 are the test conditions? Let's look to usage. For
24 medical use it specifies, yes, look, here is this
25 thing for brachytherapy. So the brachytherapy source

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1 must be tested for temperature, under conditions of 5.
2 Then 5 is the most rigorous test condition.

3 For puncture, the brachytherapy source
4 must be tested to three conditions, for impact for
5 two, vibration, no test is required. One means no
6 test. Again for reference, 5 is the most vigorous, 1
7 is no test. Puncture test not required.

8 Let's flip to the next table and I'll just
9 give you a quick flash view about what the test
10 conditions are. Remember, brachytherapy sources must
11 be tested for temperature, 5. For the minus 40
12 centigrade for 20 minutes, plus 400 Centigrade one
13 hour and then drop them into room temperature water
14 for exposing them to thermal shock. And these yellow
15 blocks indicate the test conditions for the
16 brachytherapy sources. Five is temperature, three for
17 external pressure, decrease the pressure from one
18 level to the other. No test for vibration, no test
19 for puncture.

20 For your reference, I include the table
21 for the current American standard. That is what we
22 sent to ANSI for publication this summer. And look at
23 the medical use, no brachytherapy, only radiography
24 and gammagraphy and the conditions.

25 Well, we already talked about

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1 classification here, so I quickly refresh your memory.
2 This is what you see when you have a technical
3 description or the registration for the source. It
4 references the standard, the year, the diseases that
5 it was approved for maximal radioactive material
6 content and the five conditions for tests.

7 This is important because you remember,
8 brachytherapy sources by the international standards
9 should be 5, 3, 2, 1, 1. Let's look what we find in
10 real life.

11 Both of those 22 registrations, this is
12 what I found. Some of them have this kind of
13 classification. This is less for temperature. This
14 meets exactly. This exceeds for temperature. This
15 has not been tested for impact and this has not been
16 tested for temperatures. And as you remember,
17 regulations don't require the standard. They require
18 some sort of testing and that could be entirely a
19 custom test protocol which the manufacturer proposes
20 or semi-custom. And so in some cases, there are
21 really some cost of test conditions like stepping on
22 it, or they push a cart over it, autoclaving,
23 temperature range test, they drop it from some
24 different over they have other impact tests. That
25 could be an entirely custom prototype.

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1 So that's the current situation for those
2 which exist in the registration.

3 So sum up what we said, we intended to
4 show you, you know, what is the content of the
5 registration sheet and the conditions of the use. And
6 that's how far those brachytherapy seeds can be used
7 under NRC or an agreement state life.

8 The sheets specify the conditions of use.
9 They describe prototype tests which are not
10 standardized, may be according to the standard or
11 customized. And as you see, there are no -- there is
12 no agreement for its use or for prototype testing.

13 I'd like to call to the Committee's
14 attention some facts, that there are some device
15 source specific standards, not this ISO, what I showed
16 you or the ANSI source standard because they apply to
17 everything from irradiated sources to any kind of
18 small sources, moisture density gauges and so on.
19 Maybe the specific conditions of brachytherapy sources
20 and seeds needs a specific standard. Think of one,
21 for example, for watches which have three little beads
22 in it which glow in the dark. They have those tiny
23 beads which is about 2 millimeter length, 1 millimeter
24 with tritium in it.

25 There is a standard which is called ANSI

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1 standard for testing tritium light making sources.
2 Maybe a standard like that could be applicable. I
3 don't know, but this is what I can present to you
4 about prototype testing and the registration of
5 sources.

6 CHAIRMAN MALMUD: Thank you. Are there
7 questions for Dr. Jankovich.

8 Yes?

9 MEMBER BAILEY: John, if I remember
10 correctly, the two ANSI standards have been withdrawn.
11 Had a primary concern of radium needles and existed
12 about the time when radium needles were being
13 withdrawn from widespread use and there was such
14 things as the bending test. There was concern about
15 since those sources were re-used, the autoclaving of
16 the sources for sterilization and the leak testing
17 provided alternatives to what we call the standard
18 leak test of wiping and wherein you could put the
19 needles in a container and let the radon off-gas and
20 in fact, there was a specification for radon leakage,
21 as I remember.

22 Are you suggesting that under the present
23 conditions that those same sort of standards ought to
24 apply to seeds, but because I think --

25 DR. JANKOVICH: Not at all.

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1 MEMBER BAILEY: Because traditionally,
2 we've sort of considered some of those seeds almost as
3 non-sealed sources when you get back to some of them
4 which actually were just the metal themselves.

5 DR. JANKOVICH: I am familiar with those
6 standards and you described that content exactly. So
7 again, this doesn't apply to these three millimeter
8 little-bitty sources. And maybe the Committee should
9 think about some other standards, not to revive those.
10 Or maybe some other means. Of course, ANSI is
11 representing the entire country. Anybody can go there
12 and ask them to ask for a standard and go through the
13 procedure. They put together a working group, they
14 come up with a draft that gets approved and that is
15 the standard, or other means.

16 So my purpose here is to present the
17 situation as it exists now and obviously we have to go
18 forward and find the solution. And reviving those old
19 standards which apply to big, old sources may not be
20 the way to do it.

21 MEMBER BAILEY: May I have a follow-on to
22 that? When you gave the number of SS&D sheets issued,
23 did you include those that were not AEA materials?

24 DR. JANKOVICH: No.

25 MEMBER BAILEY: Okay, so --

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1 DR. JANKOVICH: Actually, I just did the
2 search for Iodine-135 and Palladium-103.

3 MEMBER BAILEY: Okay.

4 DR. JANKOVICH: So for those materials,
5 there are only 22 registrations.

6 MEMBER BAILEY: Thank you.

7 CHAIRMAN MALMUD: Dr. Vetter?

8 MEMBER VETTER: What problem are we trying
9 to solve?

10 DR. JANKOVICH: As I understand, there is
11 consideration to use the brachytherapy seeds for other
12 use than prostate implants. For example, markers for
13 breast tumors and, so far as I see from these
14 registrations, they have -- that kind of application
15 hasn't been considered in the past.

16 MEMBER VETTER: I'm still not sure, that's
17 an application.

18 DR. JANKOVICH: Yes.

19 MEMBER VETTER: But what problem relative
20 to safety of the seeds are we trying to solve?

21 MEMBER LIETO: May I comment to that
22 because that was going to be one of my questions, is
23 that being a classical kind of a guy, I don't quite
24 understand or have a sense for the magnitude for some
25 of these metric numbers for like external pressure of

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1 a mega-Pascal.

2 DR. JANKOVICH: The ANSI standard has it
3 in both. Let me see if I have the table here.

4 MEMBER LIETO: I'm trying to get a sense,
5 is that sort of like just a tap on the shoulder or is
6 that more equivalent to maybe a 200 pound guy standing
7 on your chest? Do you understand? Because I think
8 relating to your question, Dick, is the sense that if
9 these are going to be implanted in the breast, they're
10 probably going to be more susceptible to mechanical
11 and external pressures and so forth than they were if
12 they were in the middle of your abdomen. And so if
13 you have something that can't or has never been tested
14 to survive those kinds of environmental effects, how
15 do you know you're not going to have leakage?

16 MEMBER VETTER: That gets back to my
17 question, what problem are we trying to solve? Has
18 there been a problem identified with the use of these
19 seeds for other applications?

20 DR. JANKOVICH: As I understand the
21 question has come up to use these seeds for markers.

22 MEMBER VETTER: What problem is that?

23 DR. JANKOVICH: It's up to the Committee
24 to decide here, to proceed with anything or there is
25 no problem. I can't answer that question.

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1 MR. ESSIG: If I may try to clarify, it's
2 really the subject of the presentation which follows
3 this one which talks about the implant of these
4 brachytherapy seeds and the question then came up is
5 during the surgical removal of tissues, have the seeds
6 been evaluated for puncture by a scalpel, for example?
7 The answer is no, they have not.

8 MEMBER NAG: Actually, yes. We also used
9 permanent Iodine-125 seeds for liver implant and
10 implant in other organ other than prostate, for
11 example, also in pancreas we've done it. And some of
12 the patients go back and have surgery. When they go
13 back and have surgery and if they are within the first
14 half lives, we ask that someone from radiation
15 oncology be there. So we have recovered seeds that
16 have been dissected out. No one has tried to
17 manipulate the seed, but they have dissected the area
18 out. We haven't had any nickings of the seed. We
19 take out the seed and we store them.

20 CHAIRMAN MALMUD: It appears that the
21 question that's being raised by a member of the
22 Committee is, is this information being presented to
23 us today in order for us to make a recommendation for
24 new standards for evaluating the seeds in the event,
25 well, as they are used in breast cancer patients?

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1 Is that the question before us? Or just
2 to inform us that this is happening?

3 MR. ESSIG: Well, I think it might be
4 clear if the question could be held until the
5 presentation. Keep the two of them together in mind
6 and then decide, although notwithstanding Dr. Nag's
7 comment, I don't believe this was one of the -- part
8 of the test protocol for this particular seed. And so
9 the question then comes up is it something that should
10 be considered in the form of a new standard or a new
11 test.

12 CHAIRMAN MALMUD: Thank you. In that
13 case, we'll thank Dr. Jankovich for his presentation
14 and giving us the background with regard to the seeds
15 and move on to the presentation on their use in
16 marking patients with breast cancer. If we may have
17 that presentation next, we'll hold the discussion
18 regarding both of these until the end of that
19 presentation. And that is to be made by -- this is
20 Roger Gallagher, the Chairman of the Materials Pilot
21 4 at the Massachusetts Radiation Control Program.

22 MR. GALLAGHAR: Actually, it's Robert
23 Gallagher.

24 CHAIRMAN MALMUD: I'm sorry. I stand
25 corrected, Robert.

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1 MR. GALLAGHAR: You can call me Bob.

2 CHAIRMAN MALMUD: You can call me Leonard.

3 (Laughter.)

4 MR. GALLAGHAR: Well, good afternoon. My
5 name again is Bob Gallagher. I am the Chairman of
6 National Materials Program Pilot Project No. 4.

7 Before I discuss the radiation safety
8 aspects and licensing of I-125C used as markers in
9 breast cancer tumors, I want to provide you with a
10 brief description of the Pilot Project 4.

11 This project is one of five pilot projects
12 of the National Materials Program. The goal of this
13 project is to have an agreement state or a group of
14 agreement states assume responsibility for the
15 development of licensing and inspection guidance for
16 new use material for a new modality not previously
17 reviewed and approved.

18 The lead organization is the Organization
19 of Agreement States and we're comprised of four
20 agreement state members and one NRC regional member.

21 Our first priority was to decide which new
22 use of material or new modality to pursue for
23 development of licensing and inspection guidance. To
24 do this, first we reviewed the regulatory needs
25 analyzed by the National Fuels Program Pilot Project

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1 No. 1. We then surveyed the agreement states, NRC
2 Headquarters, and the NRC regional offices. We also
3 contacted a number of major medical institutions
4 across the United States.

5 Why did we choose radioactive seed
6 localization? To begin with Iodine-125 is an Atomic
7 Energy Act material, as we heard earlier. And
8 therefore, is subject to regulation by both the NRC
9 and the agreement states. Its use in this particular
10 application does not fit into 10 CFR 35.200 unsealed
11 material, written directive not required because while
12 it is being utilized for localization of a lesion, a
13 sealed source is being utilized, not an unsealed
14 source. Nor does it fit into 10 CFR 35.400, manual
15 brachytherapy because the sealed sources are not being
16 used to deliver dose to tissue.

17 Therefore, the use of Iodine-125 for
18 radioactive seed localization fits into 10 CFR
19 35.1000, other medical uses. And finally, no review
20 by the NRC or by an agreement state have been
21 performed.

22 I'll be describing the draft of licensing
23 and inspection guidance developed by the Pilot 4
24 working group. This draft was submitted to the NRC
25 and the Organization of Agreement States on September

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1 9th of this year. We have received comments from both
2 the OAS and the NRC and are currently reviewing these
3 comments which I'll describe later in my presentation.

4 Radioactive seed localization or RSL,
5 calls for the use of currently available radioactive
6 seeds previously approved for use as permanent
7 implants for the treatment of cancerous tumors. And
8 Iodine-125C, particularly between 200 to 300
9 microcuries per seed, is implanted into a breast
10 lesion using a standard 18 gauge needle. This seed or
11 seeds in the case of irregularly shaped lesions by
12 then accurately localized by a hand-held gamma probe
13 by the surgeon. Using a technique with which surgeons
14 are familiar because of its similarity to sentinel
15 lymph node biopsy and radio-guided parathyroidectomy
16 and surgically removed along with the lesion.

17 The seed they remove may be removed from
18 the specimen in surgery or the specimen with the seed
19 can be sent to pathology for removal of the seed or
20 seeds prior to analyses of the tissue. The seeds are
21 then disposed of in accordance with 10 CFR 35.92 or
22 equivalent agreement state regulations.

23 MEMBER WILLIAMSON: Are the seeds placed
24 under some sort of image guidance? I guess this is --

25 MR. GALLAGHAR: Mammographic localization.

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1 MEMBER WILLIAMSON: Okay, so is the idea
2 to create a correlation between mammography and
3 surgical pathology?

4 MR. GALLAGHAR: The idea is to improve
5 upon a technique which is currently being used, as I
6 understand it, which is the wire guided surgery. In
7 this application, the surgeon is able to excise the
8 lesion and the seed with the lesion without having to
9 affect healthy tissue.

10 MEMBER DIAMOND: Maybe I can comment.

11 CHAIRMAN MALMUD: That is Dr. Diamond
12 speaking now. That was Dr. Williamson before.

13 MEMBER DIAMOND: Very often when a lady
14 has a suspected breast cancer, the radiologist will
15 place a metallic clip under ultrasound or mammographic
16 guidance, that is used so that when the patient is
17 taken to the operating room, the surgeon can then
18 again use that modality to help localize that area of
19 concern and what the surgeon will do, the surgeon will
20 track out the way he or she would like to approach the
21 tumor, meaning what angle through the breast. They
22 will then go and attempt to in the contiguity remove
23 the breast tumor plus a rim of normal tissue around
24 it.

25 My assumption is is that sometimes it can

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1 become somewhat difficult in the operating room to
2 bring this lady back and forth and localize where that
3 metallic clip is actually within a breast,
4 particularly if the breast is large and pendulous and
5 perhaps if one could use a radioactive marker where
6 the surgeon can use a hand-held gamma probe, in real
7 time it may make that localization process more
8 precise and quicker.

9 CHAIRMAN MALMUD: Thank you.

10 MR. GALLAGHAR: The guidance developed by
11 the working group focused on radiation safety aspects
12 of RSL. In addition to the general information
13 required for any amendments, such as radionuclide,
14 form, possession, limit and use, the licensee must
15 also submit facility diagrams which must include all
16 areas of use such as administration, excision, removal
17 from tissue, analyses and storage for disposal.

18 MEMBER WILLIAMSON: May I ask why is that?
19 For permanent seed implants that are re-used many
20 times, that activity is not required.

21 MR. GALLAGHAR: Typically, we're concerned
22 if the -- for example, the seeds are being removed
23 elsewhere to a location that's already been reviewed
24 by licensure such as an external pathology laboratory.

25 CHAIRMAN MALMUD: Does that answer your

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1 question, Dr. Williamson?

2 MEMBER WILLIAMSON: I guess I'll just
3 listen and comment later.

4 MEMBER LIETO: These are then essentially
5 the same type of seeds that are used for prostate
6 implants because didn't you say the activity is like
7 about .2 to .3 millicuries per seed?

8 MR. GALLAGHAR: Correct.

9 MEMBER WILLIAMSON: Not millicuries,
10 they're microcuries, right?

11 MR. GALLAGHAR: Point 2, to .3 millicuries
12 which is 200 to 300 microcuries, correct.

13 MEMBER WILLIAMSON: Okay.

14 CHAIRMAN MALMUD: Would those who are
15 making spontaneous comments, please advance the
16 comment with their names for the transcriptionist.
17 Thank you.

18 Dr. Nag.

19 MEMBER NAG: Actually, I had been
20 approached about this a few years ago. Basically, the
21 reason this came up was that many of the radioactive
22 iodine seeds of prostate implant were not in use for
23 prostate implant and had to be thrown away. And
24 people were thinking of ways to use these radioactive
25 seeds that were manufactured for prostate implant and

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1 that would otherwise be thrown away and could be used
2 for something useful. And that's when the idea came
3 up that why not use it to detect areas that would be
4 difficult to find otherwise.

5 A similar thing we have is when we have
6 implanted an organ with Iodine seeds and the patient
7 dies, within the first half life, what do we do with
8 the organ and this has come up several times before
9 that we then take the whole organ out and we are not
10 allowed to cremate this patient. That patient has to
11 cremate, what do you do? We take the whole organ out
12 and then we dispose of the entire organ by radioactive
13 decay. So basically, you are doing the same thing.
14 You are taking seeds that otherwise decayed down to a
15 less than useful level and what do you do with those
16 seeds afterwards?

17 CHAIRMAN MALMUD: Dr. Nag, may I ask what
18 is the current practice? What happens when the seeds
19 are in an organ in a patient who has died and the
20 organ is removed? How is that organ dealt with?

21 MEMBER NAG: We inform Radiation Safety
22 and Radiation Safety will do one of two things.
23 Either it will take the whole organ and we will then
24 store it for decay within half lives or it is in a
25 place where we can easily block out the seed. If it

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1 is in some organs, it's not possible, but if it is, we
2 block out the seed, store in a lead container for
3 radioactive decay. But we have to store it for 10
4 half lives.

5 CHAIRMAN MALMUD: Thank you. Dr.
6 Williamson?

7 MEMBER WILLIAMSON: I guess I must
8 confess, I'm quite unfamiliar with this procedure.
9 This would seem to be not a particularly wise choice
10 of source for this purpose because the radiation
11 burden to the patient relative to the useful radiation
12 output coming out of the patient that you could do the
13 localization, it would seem to me to be very high,
14 that one would think that a more appropriate choice of
15 radioactive source would be a much smaller quantity of
16 a higher energy gamma emitter that wouldn't give so
17 much radiation dose to the patient for what is
18 essentially an imaging procedure.

19 CHAIRMAN MALMUD: Dr. Nag?

20 MEMBER NAG: Yes, but that would require
21 making a new isotope and making something specifically
22 for that. These are seeds that are otherwise going to
23 be thrown away. It's something that didn't cost
24 anything to the manufacturer and now they will sell it
25 for a price.

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1 CHAIRMAN MALMUD: Is that, in fact, the
2 information -- is that, in fact, the background of how
3 these seeds will be obtained?

4 MEMBER NAG: Yes. We had been contacted
5 about three or four years ago that we have the lowest
6 seed activity. We throw them away. Can we use them
7 for some other material?

8 CHAIRMAN MALMUD: Thank you for that
9 background information.

10 Mr. Lieto, you would like to make a
11 comment?

12 MEMBER LIETO: I'll defer to Dr. Eggli.

13 MEMBER EGGLI: Typically, these seeds are
14 installed immediately before the surgery, so that the
15 radiation burden to the patient is small because the
16 dwell time is very short.

17 CHAIRMAN MALMUD: Thank you, Dr. Eggli.
18 Mr. Lieto?

19 MEMBER LIETO: That answers my question.
20 I was going to say the same thing as Jeff. I mean I
21 just can't see how the dose, this would be a lower
22 dose to the patient and compared to lymph node
23 scintigraphy, I mean they're using these probes to try
24 to -- and they're detecting microcurie amounts in
25 surgeries. So it sure seems like this is an awful lot

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1 of activity that you're using here, but if it's a very
2 short period of time, then that's another thing.

3 CHAIRMAN MALMUD: Dr. Eggli?

4 MEMBER EGGLI: The other benefit of this
5 is it allows them to encompass the entire lesion.
6 With the wire localization procedure, one of the
7 things you never know is you've taken out the wire,
8 but have you taken out the entire lesion? With the
9 seeds, you can sort of bracket the lesion and
10 therefore with the probe know that you've excised the
11 whole thing and that's the big issue for the breast
12 surgeon is to know that they've taken out the whole
13 thing. So this would represent a significant
14 improvement over wire localization where the wire is
15 typically put into the center of the lesion and the
16 surgeon has no idea what kind of a margin they've
17 achieved surgically.

18 If you take out all the seeds you put in,
19 you know you've got the lesion.

20 CHAIRMAN MALMUD: May we let Mr. Gallagher
21 continue at this point?

22 MR. GALLAGHAR: Thank you.

23 CHAIRMAN MALMUD: You're certainly
24 stimulating some discussion.

25 (Laughter.)

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1 MR. GALLAGHAR: That was my hope. As for
2 authorized users, the applicant must identify all
3 authorized users and document his or her training.
4 The authorized user will be considered qualified for
5 implantation, localization and removal of the seeds if
6 they meet either of the criteria in 10 CFR 35.490 or
7 before October 24th of this year, requirements of
8 35.940 or 10 CFR 35.290 or again before October of
9 this year, the requirements of 920, 35.920.

10 And preceptorship training by a 35.490
11 authorized user to include work experience and
12 ordering, receiving, unpacking radioactive fuel safely
13 and performing the related radiation safety surveys
14 using appropriate instrumentation; preparing,
15 implanting and removing brachytherapy sources, the
16 emergency procedures, using administrative controls to
17 prevent a medical event involving this device and
18 maintaining running inventories of material at hand.

19 General surgeons, working under the
20 direction of an authorized user described above, will
21 remove the seed or seeds with biological specimen,
22 should complete eight hours of radiation safety
23 training, in addition to specific training that
24 includes performing the related radiation surveys,
25 using appropriate instrumentation, preparing,

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1 implanting and safely removing brachytherapy sources
2 and emergency procedures.

3 This training shall be under the guidance
4 of the authorized user qualified under 35.490 or
5 qualified under 35.290 and the preceptorship training
6 I mentioned earlier.

7 As for records, because Iodine-125 sources
8 are temporarily implanted, the applicant may simplify
9 its submission by confirming that will meet the
10 brachytherapy requirements appropriate for temporary
11 implant in 10 CFR Part 35, subpart F, manual
12 brachytherapy; subpart L, record; and subpart M,
13 reports.

14 There's a question?

15 CHAIRMAN MALMUD: Dr. Williamson?

16 MEMBER WILLIAMSON: Yes, I'm confused.
17 How can these be licensed under 35.200 when it's a
18 sealed brachytherapy source. As we heard in the
19 previous discussion, even therospheres -- the
20 regulation has been modeled on 400 and the authorized
21 user is a radiation oncologist. So since this would
22 seem to be a variance with the way 35.200 is written,
23 why is this not being discussed in the context of
24 1000?

25 MR. GALLAGHAR: It is being discussed in

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1 the context of 1000. As you saw earlier in one of my
2 slides that this is a combination of both a
3 localization under 200 and a manual brachytherapy
4 under 400.

5 MEMBER WILLIAMSON: They're merging
6 technology.

7 MR. GALLAGHAR: We have to use the Part
8 1000 and like what was mentioned earlier, perhaps
9 maybe using 80 percent of 200 and maybe 20 percent in
10 the 400. So in other words, we're taking whatever is
11 applicable to each to fit into the part 1000 to
12 determine the regulatory's framework to accomplish, to
13 allow this to be used.

14 CHAIRMAN MALMUD: Dr. Nag?

15 MEMBER NAG: I would have a very similar
16 question, but you answered part of it. I would say
17 probably it should be the other way around. It had
18 more of a way 400 in terms of the radiation safety
19 because you can use 0.3 millicurie per seed and
20 implant in prostate. You just have to implant double
21 the number of seeds.

22 In terms of the radiation safety aspect,
23 is it more of the 400, if you want to have a
24 percentage I would say 80 percent of 400 and 20
25 percent of the 200.

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1 MR. GALLAGHAR: I was using the example
2 mentioned earlier, the 80 -- yes, you're right. It's
3 a combination of the two approaches.

4 CHAIRMAN MALMUD: Please continue.

5 MR. GALLAGHAR: Thank you. For the safety
6 precautions for the RSL procedures, we asked licensees
7 to provide procedures addressing safety procedures and
8 instructions, including survey procedures, specifying
9 the individuals that must be physically present during
10 implantation and removal, source accountability and
11 link testing, and verification of source activity
12 which may be accomplished by assay prior to
13 implantation or by the manufacturer's certification.

14 The applicant shall supply a copy of the
15 written procedures for responding to an abnormal
16 situation such as a source rupture or cut by a scalpel
17 during removal in surgery or in the pathology
18 laboratory. These procedures must include monitoring,
19 the implantation, explanation area following the
20 procedure and removal from tissue using
21 instrumentation appropriate for the radiation to be
22 measured, the process for restricting access to and
23 posting of the implantation/explantation area to
24 minimize the risk of inadvertent exposure from the
25 seeds; a description of the equipment and process and

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1 recovery of any dropped or mishandled seeds. At a
2 minimum, this equipment should include a survey
3 instrument calibrated to detect the seeds such as a
4 low energy gamma simulator, reverse action tweezers
5 and a shielded recovery container.

6 Patient follow-up should they not return
7 for removal of the seed or seeds, a description of the
8 length of time the seeds will remain in the patient,
9 not to exceed 5 days, and notification of medical
10 emergency of the patient prior to removal.

11 If the physical conditions of use exceed
12 those stated in the SS&D certificate, a limited scope
13 medical licensee will have had to amend its license to
14 allow for the new conditions. It should be noted that
15 some states will not allow variations and conditions
16 of use unless the original SS&D sheet is amended or a
17 custom evaluation is performed.

18 Broad-scope licensee should perform their
19 own engineering and radiation safety evaluations
20 addressing these differences.

21 As I mentioned earlier, the working group
22 has received comments from both the NRC and the
23 Organization of Agreement States on the RSL guidance
24 documents. We are in the process of reviewing these
25 comments and will incorporate them into the guidance

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1 document. In fact, we'll be holding a teleconference
2 call tomorrow when I return to discuss the comments
3 received.

4 The first series of comments from the NRC
5 primarily involve the pathology specimens. They
6 commented that the document should clearly delineate
7 the program for radioactive specimens going to the
8 pathology laboratory and the heightened potential for
9 the surgeon or the pathologist to lose or damage a
10 seed that would result in loss of control, Iodine-125
11 contamination and a possible medical event.

12 Specifically, they stated, the document
13 should clarify if tissue sent to pathology still
14 contain the seed or more than one microcurie of I-125
15 contamination, will be processed in its own pathology
16 department or sent to an external pathology
17 laboratory. The description of the radiation safety
18 program for the in-house pathology lab should be
19 provided. This program should contain the training
20 and experience requirements criteria for the
21 individual that will be the authorized user in
22 pathology; procedures to minimize puncturing the seed;
23 surveys to detect lost or leaking seeds; emergency
24 procedures, source accountability, storage, security
25 and disposal.

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1 If the licensee sends the radioactive
2 tissue sample to an outside pathology laboratory, the
3 licensee must also have a program to ensure the
4 samples are transferred to an NRC or an agreement
5 state licensee authorized to receive the seeds or the
6 radioactive tissue and the packet is prepared properly
7 for shipment.

8 The comment was also made that since the
9 use of the seeds for RSL is outside the normal
10 conditions of use described in the SS&D certificate
11 for manual brachytherapy seeds, more information is
12 necessary from the licensee. Comments state that the
13 applicant must be instructed to address why the
14 sources are safe to use in the normal and emergency
15 conditions of use associated with S35.1000 use.

16 For authorized users, the comment was made
17 that the addition of clinical experience should be
18 considered for addition to the authorized users
19 training and experience criteria. Also, they say the
20 guidance does not address the situation of the surgeon
21 becoming an authorized user which would necessitate a
22 more definitive description of his or her training and
23 experience.

24 The comment that the pathology lab is
25 expected to remove the seed from the tissue samples at

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1 at least one Part 30 authorized user should be
2 identified for the pathology laboratory and a
3 description of the training experience criteria be
4 provided for that individual.

5 The NRC commented that the guidance needs
6 to address the patient dose and regulatory issues
7 associated with the dose delivered to the patient from
8 the seeds. Because 10 CFR 35.2 does not define the
9 prescribed dose for brachytherapy sources used for
10 diagnostic purposes, the comment that the licensee
11 needs to provide a definition of the prescribed dose
12 for this procedure and commit the document to the
13 prescribed dose for each patient.

14 They go on to say that this dose should be
15 specified in terms of dose to the breast tissue in the
16 immediate vicinity of the sources and include the
17 expected time needed to deliver the dose so that there
18 is a clear delineation of how long the source will be
19 left in place and time for explanation.

20 Patient safety. The NRC also commented
21 that the guidance does not adequately convey the real
22 potential for source rupture during the procedure.
23 They go on to say that discussion should be included
24 about the possibility for pre-treatment to mitigate I-
25 125 update from a ruptured source.

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1 MEMBER WILLIAMSON: What does that mean?

2 MR. GALLAGHAR: I do want to say that we
3 did look into that very early on and in our
4 discussions with several medical institutions that are
5 doing this, they did say that they are, in fact,
6 administering thyroid blocking agents as a precaution.

7 CHAIRMAN MALMUD: Please go ahead.

8 MR. GALLAGHAR: They also identified some
9 areas that need further discussion within NRC. For
10 example, format. The NRC is currently evaluating a
11 number of different formats to determine a standard
12 format for developing guidances under 10 CFR 35.1000
13 uses. The format used in the preparation of this
14 guidance was one provided by the NRC early this
15 spring. The format to use for development of the
16 guidance document was discussed early on and we
17 decided to follow what was then the NRC's format for
18 responding to a technical assistance request. It was
19 recognized that both the NRC and the agreement states
20 may well change the format to suit their needs.

21 Submission of procedures. Reconciliation
22 is needed, not only within the NRC, but within the
23 agreement states as well on which procedures must be
24 provided under 35.12 for the NRC and which ones the
25 applicant can commit to having without submitting for

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1 review.

2 In summary, I've described radiation
3 safety aspects of Iodine-125 therapeutic seeds used as
4 markers in breast cancer tumors and the guidance
5 developed by Pilot Project 4. I've also described the
6 comments we have received from the NRC.

7 The working group received the comments
8 only recently and has not had a chance to discuss
9 their incorporation with the document. We will be
10 discussing comments tomorrow by teleconference.
11 Revised guidance will be submitted to the NRC, Office
12 of State and Tribal Programs no later than October
13 22nd of this year.

14 I'll take any questions you may have.

15 CHAIRMAN MALMUD: Thank you. First
16 question? Dr. Diamond.

17 MEMBER DIAMOND: How many institutions in
18 your region are doing this at this time?

19 MR. GALLAGHAR: In Massachusetts, none.
20 We found that the initial clinical trials have been
21 done in Florida and at the Mayo Clinics in Arizona and
22 Illinois.

23 MEMBER DIAMOND: Is this being proposed
24 that these seeds to be used to bracket the lesion and
25 then immediately go for surgical extirpation, or are

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1 there instances where they will be placed and then
2 three or four months later, then and only then
3 removed. And the reason I ask the question is that
4 ladies with breast cancer who have the surgery done
5 sometimes will go immediately to surgery and other
6 times we place radio opaque clips. The woman,
7 depending on the stage of her disease and clinical
8 status, may get three or four months of new agent
9 chemotherapy and then these same markers are used to
10 help find where the tumor bed was, because the tumor
11 can shrink, and as a surgeon, one must ensure that the
12 entire pre-chemotherapy operable bed is removed.

13 So is this being done as an immediate
14 sequence of events or is it being planned for this
15 three or four month delay process?

16 MR. GALLAGHAR: The original procedure,
17 protocol was designed for no longer than five days,
18 typically, within one to two days post-implantation.
19 The patient comes into surgery, they're explanted from
20 the patient.

21 MEMBER DIAMOND: If this is also being
22 used to bracket a tumor bed, in a woman who will be
23 receiving chemotherapy, potentially the lesion can
24 completely go away under the influence of the
25 chemotherapy. During that period of time there is a

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1 strong possibility, particularly an older lady with
2 fatty breasts that these markers can migrate within
3 the breast tissue. The clips that are used at the
4 present time by our diagnostic radiology colleagues
5 are special angle clips that are designed to help
6 provide traction, so there would be the possibility
7 that this could migrate some distance within breast
8 tissue, particularly in a woman with very fatty
9 breasts and very weak suspensatory ligaments.

10 The other thing I would like to comment is
11 that you must realize that in the typical setting the
12 surgeon removes the specimen, pulls it on out, drops
13 it in a container. You need to make sure this doesn't
14 fall out, obviously, from the specimen during the
15 transfer and the specimen is usually first processed
16 by not the pathologist, but by laboratory technicians,
17 and it's only at some later point that it actually,
18 the M.D. pathologist gets to this tissue.

19 So as you're thinking through these series
20 of events, who is handling this tissue, what training
21 is required, it needs to be very clearly thought out
22 at all points along that pathway who is actually
23 handling the tissue and recognize that this will never
24 gain any popularity if the regulations are so strict
25 that only specialized laboratories can have access to

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1 it. Those are my comments.

2 CHAIRMAN MALMUD: Thank you. Dr.
3 Williamson.

4 MEMBER WILLIAMSON: Is this currently
5 being carried out as a research study by broad scope
6 licensees using their own expended seeds or leftover
7 seeds from perhaps they haven't used for prostate
8 brachytherapy? Or is this as commercial venture being
9 undertaken by the seed vendors and manufacturers? And
10 if the latter, why aren't they maybe considering
11 amending the SDDR and providing an appropriate safety
12 analysis?

13 MR. GALLAGHAR: Currently, this procedure
14 is being done at a broad scope medical institution in
15 Florida where it began. There has been discussions
16 with the manufacturers to amend their SS&D sheet. I'm
17 not sure where that direction is going. I think
18 they're looking at their corporate crystal balls to
19 see how economically viable it's going to be.

20 MEMBER WILLIAMSON: I see. So it might be
21 that it's just something left in the province of broad
22 scope licensees, but you're considering extending it
23 to 35.1000 so that specific scope licensees can do it
24 too?

25 MR. GALLAGHAR: That's correct.

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1 MEMBER WILLIAMSON: Without an SSDR.

2 MR. GALLAGHAR: Correct.

3 MEMBER WILLIAMSON: Modification.

4 CHAIRMAN MALMUD: Dr. Nag.

5 MEMBER NAG: Does that have a maximum
6 activity that they have proposed on a say 0.12 to 0.13
7 millicurie? Have they proposed any maximum activity or
8 minimum activity yet?

9 MR. GALLAGHAR: The proposed maximum
10 activity is the .3 millicuries. Typically, as I
11 understand it, it's around the 100 microcurie range is
12 what they use for the implantation.

13 MEMBER NAG: Okay, now in the broad scope
14 outside lab, how are -- are we doing any containing,
15 are we putting in a container or anything like that?

16 MR. GALLAGHAR: Yes, that's where, as I
17 mentioned earlier in my presentation, that the license
18 reviewer would have to evaluate how that transfer is
19 being made to make sure it complies with DOT shipping
20 requirements.

21 MEMBER NAG: Now the third question is
22 that requiring a new licensee to have a license maybe
23 going a little bit overboard because you are probably
24 talking about two or three seeds at 0.1, 0.2
25 millicurie for a total maybe of less than 1

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1 millicurie. Am I right?

2 MR. GALLAGHAR: Right.

3 MEMBER NAG: We have many patients who we
4 had implanted radioactive seeds including prostate
5 seeds and in other organs who have died with a total
6 radiation activity of more than 1 millicurie because
7 of the larger activity of seed and the larger number
8 of seeds. And after they have died, they had been
9 transferred over to the funeral home.

10 The only requirement we've had is if we
11 are not opening up the organ, we are just tagging to
12 the patient a paper that says the patient has X number
13 of millicurie implanted in him and if you are not
14 doing any autopsy procedure where you are opening up
15 the area, that patient can be buried in a normal
16 fashion.

17 We are not talking about a much lower
18 quantity, less perhaps, even less than 1/10th or
19 1/100th of that and now you have an overburden of
20 having a new licensee taking over less than 1
21 millicurie seed when this is just a small amount. I
22 think you have to consider the amount of millicurie in
23 relation to what we have been doing with hundreds of
24 patients that have been transferred to funeral homes.

25 MR. GALLAGHAR: I understand. If I may,

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1 before we go on. I will say that currently what
2 you're commenting on right now is a comment made by
3 NRC to the draft guidance, this use of external
4 pathology laboratories. Currently, this is being
5 used, the pathology laboratories are located within
6 the licensee's own facility, so that has not become an
7 issue, but it is an area that we are going to be
8 looking at the guidance document to make sure it's
9 clearly stated in there.

10 Should an external facility be used, we
11 get a commitment that the proper requirements are
12 adhered to, that being the DOT requirements for
13 transport from the licensed facility to the other.

14 MEMBER NAG: For less than one millicurie,
15 do you need all that for less than one millicurie?

16 If you are having the maximum of two or
17 three seeds, what I suggest is you make a guidance
18 document for something with less than one millicurie
19 so that if you take a small and insignificant amount,
20 you would not have burdened him with paperwork.

21 If you take a large quantity, I don't know
22 why someone would want to implant 10 or 15 seeds and
23 have a total of 10, 5 or 10 millicurie. That's
24 different. But when it's less than one millicurie, I
25 think you are making it overly burdensome.

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1 MR. GALLAGHAR: Again, this is something
2 that's under discussion with the working group.

3 CHAIRMAN MALMUD: Dr. Vetter.

4 MEMBER VETTER: If I could just reflect a
5 little personal experience, since you mentioned three
6 facilities by name.

7 (Laughter.)

8 The seeds are 100 microcuries. They are
9 usually one or two seeds, occasionally three. It's
10 used primarily to replace the wire so that the surgeon
11 can more accurately pinpoint the lesion and there's
12 considerably more tissue sparing during surgery as a
13 result of that as opposed to tracking that wire. So
14 they are much more satisfied with the surgery.

15 The seeds are removed in surgery. It
16 wouldn't have to be -- I mean a licensee could do, as
17 you suggested, they could send it to the pathology lab
18 and they could be removed there, but we remove them in
19 surgery. They do not -- so when the tissue goes to
20 the lab, the pathologists scan it and it's cold.
21 There's never been a problem with the surgeon trying
22 to locate. In fact, when they're teasing with their
23 scalpel, they can easily find the seed. They're not
24 going to cut through a seed. That would be very
25 unusual. And surgeons have really liked it.

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1 One question I have is what, it's sort of
2 a rhetorical question. What training would you give
3 a surgeon, using this technique, that would take eight
4 hours?

5 I mean the amount of training the surgeon
6 needs to do this is about a half hour. They need to
7 know what they're looking for, what the consequences
8 are and what they have to do, where to put it when
9 they're done or where the surgical tech puts it when
10 they're done. It's really very, very straight
11 forward.

12 MR. GALLAGHAR: I understand. We actually
13 talked about that very issue, how much training to
14 provide the general surgeon. Someone at the working
15 group wanted to have it at a minimal, as you say.
16 Others wanted to go for much much longer.

17 It actually came up in the discussion.

18 CHAIRMAN MALMUD: Dr. Eggli.

19 MEMBER EGGLI: It seems to me that the
20 biggest risk here is breaking one of the seeds. Can
21 you cut a seed with the scalpel?

22 MEMBER VETTER: I never tried to. I
23 suppose you could. You are more likely to cut it with
24 scissors.

25 MEMBER NAG: Can you? I guess if you

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1 tried really hard enough, you could. I mean we had
2 tried, not that it happened. The only time you can
3 really do it if you're using a scissors and you're
4 inadvertently trying to cut it. The only other time
5 you can break it is if you are having an applicator
6 where you having it direct and once you push it
7 doesn't go, you keep on hammering at it. You can
8 break it.

9 MEMBER DIAMOND: Well, what about, what
10 about if you're using a Bovi electrocautery device.
11 Most of these operations are not -- after you make the
12 skin incision are done with a Bovi. And for those of
13 you who have never seen one, it's an electron scalpel
14 that has this cutting with an electric current, will
15 actually go and cauterize the small vessels, so you're
16 actually going around the tissue in a three-
17 dimensional manner, trying to get a spherical of the
18 tissue. What happens if you take that Bovi and make
19 contact with one of these little metallic seeds? That
20 actually is the most likely scenario.

21 CHAIRMAN MALMUD: Yes.

22 MR. GALLAGHAR: Could I respond to some of
23 these comments? I want to say that we did look into
24 not only did we do an End Med search to see if
25 historically what kind of damage has been done to

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1 those brachytherapy seeds overall, and I reviewed
2 personally all the cases that were reported to End
3 Med, and as you say most of them did involve either a
4 crushing injury of some sort or scissors. We were
5 unable to find that involved surgery, scalpel.

6 I did talk to colleagues at Mass. General
7 Hospital that use this procedure routinely, not only
8 for prostate, but they have had occasion to surgically
9 remove a seed of this sort and they also have not had
10 any problems with any leakage.

11 They went on to voluntarily quote test
12 this, by implanting some live seeds into chicken
13 breast tissue and then surgically remove them under
14 not laboratory conditions, I can say, but they
15 certainly did try to apply as much force as they could
16 and then they leak-tested the sources and they did not
17 fail.

18 CHAIRMAN MALMUD: Thank you. We do have
19 some questions from the floor from others, members of
20 the ACMUI.

21 May we entertain those now?

22 MR. ESSIG: Your choice, Mr. Chair.

23 CHAIRMAN MALMUD: Yes, please. Would you
24 please introduce yourself.

25 DR. WHITE: I'm Jerry White. I'm here as

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1 a representative of the AAPM, although my comments are
2 strictly personal, as a medical physicist and an RSO,
3 contemplating this procedure in the future.

4 One of the things that I think as this
5 rolls out, that is an important difference between the
6 way it's handled now in large facilities, and in large
7 active, community hospitals like ours, is that this
8 procedure is seldom done in a single facility start to
9 finish.

10 A more common model is radiation oncology
11 or authorized user, you have a mammographer who may or
12 may not be in the hospital. Could be in a free-
13 standing center. And then a free-standing surgical
14 center and then another pathology facility. And
15 effective administrative control over the seeds from
16 all of those, to all of those different facilities in
17 the community setting is virtually impossible. The
18 economic pressures are enormous.

19 And if this rolls out to the community
20 hospital, the regulatory structure really must have
21 some structure that is more powerful and I know -- I
22 have great respect for the power of regulators, more
23 powerful than the economic pressures that we face when
24 dealing with surgeons and pathologists and disparate
25 institutions. I think that's not to be trifled with.

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1 And I also just can't -- several people
2 talked about breakage of seeds and scalpels. We also
3 have microtones involved, seeds that might end up --
4 the surgeon thought he has removed. Ten surgeries
5 that day. You need to get them all done. Got to rush
6 to the next patient. I'm sure I counted all the
7 seeds. And the pathologist runs it through an
8 autoclave. The contamination problems with I-125 are
9 significant. It's got a long half-life. It goes to
10 the thyroid. It's got a low ALI. There's a potential
11 if these seeds are cut and there are a lot of knives
12 in this process, I think to be a real issue.

13 I just wanted to be nervous in front of
14 all of you about this.

15 CHAIRMAN MALMUD: Thank you. Is there
16 another comment?

17 DR. JANKOVICH: This is John Jankovich
18 from the NRC. I'd like to make a comment on the
19 question which was raised here a few minutes ago, if
20 the seeds can be damaged by scalpel. NRC has a
21 contamination case on their re-investigation. This
22 was a strand manufacturer, melted, biodegradable
23 material around these seeds and made a strand several
24 units long and how they were making it on a flat tray
25 and there were rolls of seeds and they pulled the

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1 plastic over it and they separated individual strands
2 by cutting them into long strips. And there is an
3 indication that some seeds were damaged and they got
4 into the patient and we have contamination.

5 The case is not closed yet. I cannot tell
6 more about it. This is our early indication.

7 CHAIRMAN MALMUD: Thank you, Dr.
8 Jankovich.

9 Any other comments from the floor? If not, we'll
10 return to the committee.

11 MEMBER LIETO: Dr. Malmud, a quick
12 question for Mr. Gallagher.

13 Have you received any comments from the
14 agreement states on this proposed guidance?

15 MR. GALLAGHAR: We have received comments
16 from the Organization of Agreement States, yes. And
17 they were more editorial in nature.

18 MEMBER LIETO: Thank you.

19 CHAIRMAN MALMUD: Mr. Bailey?

20 MEMBER BAILEY: Bob, are there any
21 indications that this -- the use of these seeds could
22 be extended to tumors other than breast cancer?

23 MR. GALLAGHAR: Yes.

24 MEMBER BAILEY: But would you mind
25 commenting on that?

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1 MR. GALLAGHAR: I know from having
2 discussions with a number of institutions around the
3 country, as I said, that there has been some interest
4 in this use of these seeds and other tissues
5 throughout the body. Not being a physician, I'm not
6 going to say exactly where, although I do know that
7 there is some interest in this overall for other areas
8 in the body.

9 CHAIRMAN MALMUD: Thank you. Any other
10 comments from members of the Committee?

11 Mr. Lieto?

12 MEMBER LIETO: I wanted to ask Mr.
13 Gallagher, was one of the purposes of your
14 presentation here that we could comment on all of
15 these various items or was it more informational for
16 us that this is being considered, we may be coming
17 back and proposing specific guidance.

18 MR. GALLAGHAR: Yes, this is, for your
19 information, this is where the guidance -- the
20 guidance is in its draft stage right now. It's under
21 review. It's been -- we've had comments back from NRC
22 and from the OAS. It's also been provided to the
23 CRCPD as well.

24 MEMBER LIETO: Final question, has anybody
25 actually taken all these radiation safety

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1 considerations and written up procedures and actually
2 go through all this from insertion to excision to
3 pathology lab and so forth?

4 MR. GALLAGHAR: As I understand it, this
5 is currently being done in Florida. And it's been
6 licensed by the State of Florida recently, so that all
7 has been submitted to the State of Florida, reviewed
8 and approved.

9 CHAIRMAN MALMUD: Dr. Diamond, you are
10 from Florida.

11 MEMBER DIAMOND: I am, indeed. I think it
12 would be very hopeful if we could get copies of the
13 research protocols that this is being done under and
14 as we review how these institutions are proceeding,
15 that would be very informative.

16 The second issue is I still would stand by
17 my thought that much more likely than a seed being
18 punctured or damaged by scissor or by cold scalpel
19 steel would be an electrocautery device coming into
20 contact with one of these metallic seeds and as you
21 know, that can generate extremely high temperatures.
22 It would be very useful to ask the vendor have they
23 ever explored what would happen if one of these
24 electrocautery -- because again, what are you trying
25 to do? You have a sphere of tissue you're trying to

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1 remove and you're going to have an array, if you will,
2 of these metallic seeds. And after you go along, it's
3 very possible to make contact with that. That's
4 probably the most likely real case scenario and
5 probably the one most likely to generate excessive
6 conditions.

7 MR. GALLAGHAR: I understand. I'll take
8 that under consideration.

9 CHAIRMAN MALMUD: And the Iodine will
10 volatilize.

11 I think that Dr. Williamson was next. Did
12 you still wish to make a comment?

13 MEMBER WILLIAMSON: I guess I'll make a
14 comment.

15 CHAIRMAN MALMUD: why not?

16 MEMBER WILLIAMSON: I'm never at a loss
17 for words. Well, I think that any realistic protocol
18 has to take into account that these are quite fragile
19 seeds and in my experience it's quite easy to rupture
20 them, although I think the risk is more from sheer
21 forces than direct puncture. So a thought would be to
22 make sure that the patient, who would be the primary
23 individual at risk, is safeguarded from a puncture or
24 leak.

25 Other than that, Iodine seeds are in many

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1 ways are among the more innocuous of the radioactive
2 materials that we do have. If they are lost or one
3 loses control of one or two very low activity seeds,
4 so you might consider tempering your recommendations
5 of what to do downstream from the patient with
6 consideration of what really the risk is, worse case
7 scenario.

8 MR. GALLAGHAR: Well, let me just say for
9 the presentation today, I had to kind of summarize our
10 guidance document and then I wanted to have time to
11 present information on the comments we've received
12 from NRC.

13 I will say that we went into detail about
14 protecting the patient. And the fact that the NRC had
15 no comments on that, I think speaks for itself. But
16 that is adequately covered in the guidance document.

17 CHAIRMAN MALMUD: Your comments were with
18 respect to protecting the patient, is that what you
19 said, the patient? What about the health care
20 workers, the nurses, the pathology workers, morticians
21 in the event that the patient had that fate and those
22 are the issues that you're presenting to us, clearly,
23 in addition to the others for our consideration.
24 Though the primary concern is always the patient.

25 MR. GALLAGHAR: Right.

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1 CHAIRMAN MALMUD: Dr. Nag.

2 MEMBER NAG: I think we will have to keep
3 things in perspective in that the maximum activity
4 from what I have heard now would be about 0.3
5 millicuries. What happens when you inject
6 purposefully 0.3 millicuries of Iodine-125 into a
7 patient? How much of that is uptake -- how much of
8 uptake is the thyroid and what bad effect does it
9 have? Zero point three millicurie, if you inject
10 purposely is not of any consequence. Then I think we
11 are making a mountain out of a mole hill. I think we
12 have to find that out first, what is the maximum
13 millicurie you are going to use on the patient and
14 what is in the worse case scenario, what is the bad
15 effect on a patient?

16 Quite simply, I contend that putting 0.3
17 millicurie of Iodine seed in a patient is not going to
18 have adverse consequence on a normal place. That's
19 not something that has me worried, if I had the seed
20 encapsulated, even if someone ought to remove the
21 seed, or the seed for some reason was not removed,
22 that is not an adverse consequence.

23 But if the seed was open and that 0.3
24 millicurie were to end up in the thyroid, would it
25 cause any problem? That's something you can find out

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1 firsthand.

2 CHAIRMAN MALMUD: There was one more
3 question, I thought.

4 Mr. Lieto?

5 MEMBER LIETO: Yes, it's kind of a little
6 bit of follow-up to what Jeff was talking about in
7 that I think there's -- when you address this, this
8 modality, it seems like you have a lot more than what
9 is even involved for putting manual, sources manually
10 into prostates.

11 And I would -- where more seeds are being
12 involved and so forth, and I would kind of maybe use
13 that as sort of maybe a template, as you're going
14 along through this process of what you're going to be
15 requiring or recommending for individuals who want to
16 use this process because verifying the source
17 activity, doing individual dose definitions, I really
18 don't understand what the value of all that is going
19 to be when these things are pre-fixed, you know, right
20 up front. I mean it's not going to vary, even if you
21 have two or three seeds. It's going to pretty much be
22 the same. And I think to have everybody that's going
23 to do this jump through some of these hoops, just to
24 document something that once you know it is not going
25 to change, I really would kind of precaution you on

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1 that.

2 I think they've already addressed -- right
3 now, we don't require training of the urologists that
4 you're requiring for the surgeons here and urologists
5 are doing the prostates. There's not that requirement,
6 so why put that on the surgeons?

7 So just some things you might, as you go
8 along, try to have things maybe sort of similar on
9 what you're requiring for prostate implants that
10 you're going to require for this.

11 CHAIRMAN MALMUD: You've given us a lot to
12 think about. Have you completed your presentation?

13 MR. GALLAGHAR: Yes.

14 CHAIRMAN MALMUD: You've given us a lot to
15 think about. This is an interesting application.

16 What makes me anxious, if I may use the
17 Chairman's prerogative to make a comment, what makes
18 me anxious about this is the use of an isotope by
19 members of the public who are not knowledgeable of the
20 risks involved in handling radioactive material and
21 the certainty that one of these, one or more of these
22 seeds will be lost, particularly given the background
23 which includes the possibility that the implantation
24 may be at one site, the surgical removal at another,
25 the absence of a surgical removal possibility, the

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1 zapping, if you will, of one of these seeds in the OR,
2 with volatilization of a small amount of I-125,
3 perhaps by a woman who is a nurse at the end of her
4 first trimester of pregnancy, the consideration as to
5 what would happen to the fetal thyroid in that case.
6 There are many things for us to consider.

7 And we need an opportunity to do those
8 things. We don't have the dosimetry at our
9 fingertips, but we do know that the radiation burden
10 would be low, low radiation burdens are not acceptable
11 to fetuses in our minds until we convince ourselves
12 that they are and there's a lot for us to work on and
13 we'll all have to deliberate on this with more facts
14 at hand.

15 But you've certainly given us the
16 background with which we can work to come to a
17 recommendation.

18 Did I summarize -- well, I think Dr.
19 Vetter wanted to speak next and then --

20 MEMBER VETTER: I'd just like to make one
21 final comment and that is that this procedure is
22 spoken of very highly by the breast surgeons. I think
23 it has significant benefit for subpopulation and we do
24 need to be careful that we don't do -- prescribe
25 regulations in such a manner that would discourage

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1 this very positive use.

2 On the other hand, once the use gets out
3 of the control of a facility where everything is done
4 basically in-house, it's very easily controlled there.
5 Once it gets into the community, as Jerry White was
6 mentioning, controls certainly are very, very
7 necessary in order to prevent any of these adverse
8 events. So I guess the point I'm making is we need to
9 strike a proper balance here. We don't want to
10 discourage the technique. On the other hand, we do
11 need proper controls.

12 CHAIRMAN MALMUD: I think that Dr.
13 Suleiman was next and then Dr. Nag.

14 MEMBER SULEIMAN: My take on it is you're
15 using an approved product. The patient risks from my
16 perspective are minimal. This is a therapy patient.
17 The training for the user should be minimal, but
18 shouldn't be zero. I see a real potential for this
19 thing expanding beyond one facility and if people
20 develop a flippant attitude, safety concerns could
21 come to play with loose seeds and outside facilities
22 where people say oh, it's not -- it's of no concern.

23 So I think nothing is new here. It's just
24 a case of pulling the appropriate controls from the
25 various other nuclides where you have similar

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1 experience.

2 MEMBER NAG: Just a comment partially for
3 Dr. Lieto. When the urologists are involved in a
4 prostate implant that you have separate radiation
5 training, but it is always done in conjunction with an
6 authorized user, that is a radiation oncologist.

7 Similarly, when our surgeons, when we do
8 implants in the liver with radioactive Iodine seeds or
9 implant in other organs, with the surgeon, they don't
10 have the radioactive training, but we do and we are
11 there, so that even if he's facing an operation and
12 the patient dies, we follow the patient or we go to
13 the OR and we tell the surgeon what not to do and what
14 to do. There is a big difference.

15 Here, if an authorized user was there, for
16 example, if we said that the seed is being inserted
17 with the help of an authorized user, I have absolutely
18 no problem if the surgeon has no training at all. The
19 authorized user is present and will guide the proper
20 radiation precautions.

21 CHAIRMAN MALMUD: Thank you, Dr. Nag. If
22 we may, yes, Tom?

23 MR. ESSIG: I just wanted to come back to
24 the comment that was made earlier by Dr. Vetter,
25 following the previous presentation and you recall I

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1 said that we would hear Mr. Gallagher's presentation
2 and then maybe try to draw the issues together.

3 The previous presentation pointed out that
4 the existing ANSI standards for these sources do not
5 involve a puncture test. And I think based on the
6 dialogue we've had around the table, perhaps a
7 surgical puncture with a scalpel may not be a major
8 issue, but Dr. Diamond noted that certainly an
9 electrocauterization was a very real possibility.

10 So it seems to me the question is that we
11 would pose to the Committee is would it be -- if we
12 have an SS&D certificate, needs to be modified, it
13 needs to be modified in some particular direction to
14 incorporate some existing -- to address some existing
15 standard and while that standard right now doesn't
16 talk -- doesn't address these additional tests, I mean
17 beyond puncture and talking about particularly the one
18 that Dr. Diamond has raised, so I'm just raising this
19 -- is there any sense that it would be worthy of
20 modifying a standard or seeing there's interest in
21 modifying a standard to incorporate the additional
22 test to assure ourselves of the safety of these -- of
23 the various surgical processes that would involve
24 these seeds.

25 CHAIRMAN MALMUD: Dr. Williamson, do you

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1 care to respond to the question?

2 MEMBER WILLIAMSON: Well, I mean if this
3 is going to become a widespread use of this product,
4 it seems a reasonable step to undertake. I think the
5 maybe more interesting question is, the more difficult
6 question is is who should do it? It seems to me this
7 is the sort of standard-setting activity that would
8 require a lot of back and forth and dialogue among the
9 vendors, agencies, different sectors of the community
10 and it's probably best done within the context of an
11 organization like ANSI or ISO and not by the NRC or
12 the FDA, but you know, be done in some sort of a forum
13 that builds in input from all of the involved sectors.
14 So I think to encourage them to do it would be a
15 reasonable step.

16 On the other hand, it sounds like this
17 particular initiative is being taken on with the
18 presumption that this is going to be done under
19 35.1000 and that one of these exemptions from the
20 existing rule language is that an SDR is not going to
21 be required. That seemed to be an assumption, I
22 thought that you -- that Robert's presentation made
23 basically.

24 MR. GALLAGHAR: Well, we have approached
25 some of the vendors, specifically one of the vendors

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1 out in Illinois to see if they're interested in doing
2 a modification to both their SS&D sheet and the 510K
3 authorization as well.

4 Likewise, we also recognize that these
5 facilities may want to do that so it may want to use
6 this material in advance of that, so we've been
7 working with the NRC to see if there's a way to do
8 that. One avenue, as I understand it in the SS&D
9 review process, is use a historical information on how
10 these devices or sources stand up under the conditions
11 to be expected. So we're pursuing that as well.

12 CHAIRMAN MALMUD: Ralph?

13 MEMBER LIETO: I guess I would ask Tom,
14 would you want a formal recommendation from this
15 Committee that the SS&Ds need to be modified or need
16 to address testing that includes common medical events
17 in their temperature pressure impacts? In other words
18 the whole gamut of categories? Is that one of the
19 things that would -- that's being asked of us?

20 I agree with Jeff. I don't know whether
21 to say it should reach Category 3 in this task or is
22 it more appropriate that it be category 5 and just
23 don't have the experience for that. I mean you'd like
24 to say 5 across the board for everything. You know
25 it's not going to be a problem, but I'm sure as heck

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1 it would affect the dosimetry distribution of the
2 sources. So I kind of -- I'm supportive of us making
3 a recommendation, but I'm not really sure where we,
4 how we want to couch this.

5 CHAIRMAN MALMUD: Dr. Diamond?

6 MEMBER DIAMOND: To respond to your
7 question and Ralph's comment, I think the appropriate
8 way to proceed is before making any recommendation as
9 to what degree of confidences we have in these small
10 seeds with respect to puncture or temperature, let's
11 go get copies of the protocol that these are being
12 done under, let's learn about exactly how these
13 operators are doing it. Are they having any specific
14 requirements made, but they're not allowing
15 electrocautery. It's a non-issue. So I think the
16 best next step is to simply get a little bit more
17 information and then we can go on and make a
18 reasonable recommendation.

19 CHAIRMAN MALMUD: So the consensus of the
20 Committee appears to be that we need a little more
21 data and then the opportunity to review what is a
22 potentially valuable surgical technique and then to
23 make a recommendation.

24 MEMBER DIAMOND: So this would be a
25 follow-up item then?

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1 CHAIRMAN MALMUD: This would require
2 follow-up, but we do need some more data when you
3 point out to us doesn't exist right now. So that
4 would be the Committee's recommendation.

5 Does someone wish to make that
6 recommendation?

7 MEMBER DIAMOND: I so recommend.

8 CHAIRMAN MALMUD: Seconded by Dr.
9 Williamson. Motion by Dr. Diamond, seconded by Dr.
10 Williamson. Any further discussion?

11 MR. ESSIG: Just one point. We have to be
12 mindful in any review that's done and I agree, it
13 needs to be done, that we are -- it was mentioned as
14 in the opening slide that there are five pilot
15 projects. Pilot number 4 got off to a very slow start
16 and so it's lagging the others considerably. All five
17 are supposed to go to the Commission very, very
18 shortly.

19 November 8th. And so I don't believe
20 there will be time to review this specific guidance
21 and have anything on paper, but if it was done at a
22 later date with the understanding that all guidance is
23 always revised, we do the best we can with the
24 information we have and so this would go to the --
25 this would go, be appended to the Commission paper.

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1 We share it with them and receive some additional
2 feedback from them, if any, and then the Committee
3 could undertake it as a separate project and provide
4 guidance.

5 That seems like a reasonable approach.

6 MEMBER BAILEY: My understanding of the
7 report that was going forward is really more -- rather
8 than to be adopted per se was that it was to
9 demonstrate that this process could work in developing
10 guidance, not that this guidance coming out of it was
11 specifically the guidance that NRC was going to adopt.
12 So I think there's plenty of time after it goes
13 forward to comment on it.

14 CHAIRMAN MALMUD: Excellent point.
15 Therefore, the final recommendation from the Committee
16 is that we will reserve our comment for the time
17 being? Are we being asked to approve of something
18 without the database? No. I know the answer to the
19 question, I just wanted to put it on the table. So
20 therefore, what -- do we stand by our previous motion
21 and second? Dr. Williamson? That's our
22 recommendation and we regard this as a potentially
23 valuable technique and wish to investigate it further,
24 have more data.

25 Thank you.

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1 Thank you, Mr. Gallagher. You generated
2 a lot of interesting discussion.

3 MR. GALLAGHAR: Thank you.

4 CHAIRMAN MALMUD: We may now, if you will,
5 move on and --

6 MR. ESSIG: Mr. Chairman, the question
7 becomes we had been scheduled for a break at 3.

8 CHAIRMAN MALMUD: Yes.

9 MR. ESSIG: The next presentation is
10 scheduled for one hour, whether or not it takes that
11 or more even --

12 CHAIRMAN MALMUD: Can we take a 10-minute
13 break?

14 We'll be back at 3:25.

15 (Off the record.)

16 CHAIRMAN MALMUD: The next presentation
17 will be by Dr. Sherbini. It will be entitled "Staff
18 Findings and Follow-up to the ACMUI Report on the NRC
19 Method of Dose Reconstruction." Dr. Sherbini will
20 present the NRC staff response to the ACMUI's
21 recommendations relating to the staff's method of
22 reconstructing doses.

23 And with that introduction, I think I
24 brought you all back to the table. Dr. Sherbini,
25 you're on.

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1 DR. SHERBINI: Thank you, Dr. Malmud.

2 If I might correct the statement you just
3 made, this is really a response to the ACMUI report.
4 It's just, I guess, a summary of where we stand, what
5 we've learned from it, and our conclusions based on
6 that case. So it's really not going to address the
7 ACMUI report directly.

8 For the benefit of members of the public
9 who might not know about this case, I've prepared a
10 short background summary of the case. This case
11 occurred about two years ago at the St. Joseph
12 Emergency Hospital in Ann Arbor, Michigan. It's a
13 very large hospital, about 500 beds.

14 The case involved a patient who was
15 hospitalized for treatment for thyroid cancer, and it
16 involved exposure of 35 members of the public who
17 visited the patient during her period in the hospital,
18 which was about a week. Some of these people were
19 believed to have exceeded the acceptable limit, which
20 at the time was 100 millirem, and one of them was
21 believed to have exceeded the dose limit by at least
22 a factor of ten.

23 The licensee notified the NRC in August
24 about the incident, and the NRC conducted a special
25 inspection in October of the same year, and the

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1 inspection report was published in December, about six
2 months later.

3 In that report the NRC detailed what it
4 did and its dose assessment, and it also reported the
5 licensee's dose assessment, which was three to six rem
6 for that most highly exposed individual, whereas the
7 NRC's estimate was 15 rem.

8 Both estimates used the same methods of
9 assessment. The only difference was the estimated
10 hours of exposure that resulted in that dose. One was
11 40 by the licensee and one was 77 by the NRC.

12 A year later after the report was
13 published, was issued, the Society of Nuclear Medicine
14 sent a letter to the NRC Chairman indicating concern
15 that the NRC had grossly overestimated the dose. The
16 letter was accompanied by a proposed reconstruction
17 which concluded that the dose was closer to one rem
18 rather than 15.

19 The Commission directed us to charter
20 ACMUI to look into this, to do an independent review.
21 The NRC staff also did their independent review.
22 ACMUI submitted the report to us on May 2004, and we,
23 in turn, submitted our report to the Commission, which
24 included a review of the ACMUI report in June of this
25 year.

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1 The conclusions we drew in our report was
2 that NRC -- basically we concluded that the Region
3 III's estimate, 15 rem, is still we think the most
4 probable and the best estimate for this case. ACMUI's
5 estimate was not very far off, nine rem, using the
6 assumptions that NRC used, basically that the exposure
7 duration was close to 77 hours; that the person
8 exposed did not have the benefit of shielding, and so
9 forth.

10 If the benefit of shielding is introduced,
11 ACMUI found a dose of four rem, which is closer to the
12 licensee. So there is consistency here.

13 The outcomes of this were, I think,
14 beneficial to us because the ACMUI report, as well as
15 the ultimate dose reconstruction which was prepared by
16 Drs. Marcus and Siegel, pointed out quite a few areas
17 in which the NRC probably should have done better than
18 it had. Most of the areas had to do with preparing
19 the report in a way that would be clearly
20 understandable to the public with all of the
21 assumptions and approximations clearly and explicitly
22 stated. We didn't do this as well as we might have,
23 and that might have included some of the questions
24 anyway.

25 As a result of that, we have started

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1 several steps, actions, to correct some of these
2 weaknesses. One of these was to institute a
3 headquarters review of all inspection reports that
4 involve dose assessments. Most of these reports would
5 be created by the regions, and the purpose here is not
6 to check on the regions, but basically to look at the
7 final report from the point of view of people who
8 don't know much about the case.

9 We found from this case that people who
10 are close to the investigation generally make
11 assumptions and approximations that they think are
12 obvious and so need not be stated, and this has caused
13 problems.

14 And so we would be looking for this kind
15 for thing. We would be looking for unstated
16 assumptions, approximations, data that was assumed but
17 not reported, and so on. And the idea is to make the
18 report stand alone and everything that is done in the
19 report would be obvious and clear so that anybody who
20 reads it will understand what went on, not necessarily
21 agree with it, but at least understand it.

22 We also plan to issue a generic
23 communication to the licensees to describe generally
24 the case and the difficulties we encounter and to
25 provide some hints or ideas on how to make sure that

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1 data would be available in the future in case those
2 reconstructions may be needed.

3 Another action we're taking is to issue
4 guidance to licensees on how to assess effective dose.
5 This was a big issue in this investigation, and it was
6 raised by Drs. Marcus and Siegel and was also raised
7 by ACMUI, and it's a valid issue and it's a difficult
8 one. And we are now working on coming up with
9 reasonable guidance on how a licensee doing surveys in
10 a patient's room might get a reasonably good
11 approximation of the effective dose that a visitor
12 might receive under these conditions, especially that
13 typically the visitors would not be monitored, and so
14 the survey day would be probably the only data that's
15 available to assess that.

16 And so we're working around that idea, and
17 hopefully we should have something within a few
18 months.

19 Another thing that was pointed out by the
20 ACMUI, and we're working on that, was to come up with
21 methods that would allow the regions to permit
22 licensees to allow members of the public to be exposed
23 to doses much higher than is currently permitted,
24 which is 500 millirem without any special exemptions.

25 And so the Commission has directed us to

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1 explore different ways that we might do that: license
2 conditions, changes in the regulation, other ways that
3 would efficiently, quickly allow licensees to go up
4 much higher than 500 millirem if the conditions make
5 it necessary to do so.

6 We're not sure how we're going to do this
7 yet, but we are working on it.

8 A lot of these issues that came up, the
9 effective dose and so forth, the relationship between
10 deep dose and effective dose which came up in the
11 ACMUI report and was brought up by Drs. Marcus and
12 Siegel, we plan to offer what we call advanced
13 training in these concepts, what they mean, how they
14 can be implemented, what are the difficulties and
15 approximations, and so forth, and the training would
16 be offered to the technical staff at headquarters and
17 in agents. That's a fairly long-term project, but we
18 have started working on that and developing the
19 outlines of such a thing.

20 That's all I have, if there are any
21 questions.

22 CHAIRMAN MALMUD: Thank you, Dr. Sherbini.

23 Are there any comments or questions for
24 Dr. Sherbini? Dr. Vetter.

25 MEMBER VETTER: Relative to your thoughts

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1 about increasing allowable doses to members of the
2 public, I assume you're familiar with NCRP Commentary
3 11.

4 DR. SHERBINI: Yes, I have.

5 MEMBER VETTER: Okay, and they actually --
6 the NRC regulations currently do follow that to some
7 extent, allowing medical facilities to release
8 radioactive patients who could in such release result
9 in a maximum of 500 millirem to a member of the
10 public.

11 DR. SHERBINI: Yes.

12 MEMBER VETTER: But they also have a
13 paragraph that says to family members. It could be
14 expanded to focus on, you know, caregivers
15 specifically. To family members, it could be raised
16 to five rem contingent on the family members being
17 trained and monitored.

18 DR. SHERBINI: Yes.

19 MEMBER VETTER: And I would suggest that
20 that would be something that we should seriously
21 consider.

22 DR. SHERBINI: These are the dose levels
23 we're contemplating actually, and the Commission did
24 not place any upper limits to what the dose should be
25 that can be allowed, and so that's really quite open

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1 at this moment.

2 CHAIRMAN MALMUD: Any other comments or
3 questions? Mr. Bailey.

4 MEMBER BAILEY: If I'm remembering
5 correctly, Carl Paperiello said that NRC had allowed
6 more than 500 millirem on certain licenses.

7 MR. ESSIG: Yes. Yes, they had.

8 MEMBER BAILEY: So you will already
9 entertain that, I guess.

10 MR. ESSIG: Yes.

11 MEMBER BAILEY: Okay. I just --

12 MR. ESSIG: The difference I would comment
13 here is that the exemption that we had previously
14 entertained was for a situation which was known about
15 well ahead of time, and in one particular example that
16 comes to mind, the licensee had asked for an
17 authorization I believe up to the occupational dose
18 limit of five rem, and we ended up approving two rem,
19 and it was for a mother who was giving care to her
20 daughter.

21 And the licensee just described the
22 situation as that the regulatory requirements are just
23 too constraining. We need authorization to go up to
24 some higher value.

25 We had originally considered that why not

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1 just consider this occupational exposure. I mean, we
2 have volunteers in hospitals who aren't compensated,
3 but yet they could perhaps receive occupational
4 exposure, and where we got into a problem there is
5 that the way occupational exposure is defined in Part
6 20. Just this use of it was not -- our Office of
7 General Counsel thought that this use of it was not
8 really authorized, and so then we had to go back to a
9 case specific basis.

10 But I think the recommendations of the
11 committee on this score were well taken in that when
12 we have situations like this, we need to move very
13 rapidly. I mean there are emergent situations, and I
14 kind of liken it to in Part 20 right now. We have a
15 provision for a planned special exposure where for
16 occupational now a licensee can call and seek counsel
17 from the regional office on the planned special
18 exposure. We rarely use them, but the regulations
19 provide it.

20 This would kind of be done in the spirit
21 of that where the licensee could consult with the
22 regional office and they'd operate within some
23 framework that would be prescribed in the regulations,
24 and we would propose such to the Commission and see
25 their approval perhaps among a couple of options that

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1 we might propose.

2 CHAIRMAN MALMUD: Thank you.

3 Any other comments or questions?

4 MEMBER SULEIMAN: I mean, I'm just going
5 to reiterate what Richard had said earlier. I mean at
6 the last meeting you mentioned NCRP Commentary 11, and
7 I got a copy of it. I think we're moving towards
8 suggesting what's already been thought out and spelled
9 out here.

10 I would strongly encourage the NRC to just
11 codify that, you know, in addition to your general
12 population, your occupational worker. You know, it's
13 spelled out right here. I wouldn't take time to read
14 it, but I think it's under 5.3.3 in the NCRP
15 Commentary No. 11. I think it was published in '95.

16 So that was probably after your last round
17 of rulemaking.

18 CHAIRMAN MALMUD: Thank you, Dr. Suleiman.

19 Did you wish to respond to Dr. Suleiman?

20 DR. SHERBINI: No. I was just going to
21 note that really the difficulty is coming up with an
22 efficient mechanism rather than coming up with a dose
23 number. The dose numbers, there are quite a few
24 documents as we pointed out that recommend doses that
25 are high enough to serve the purpose, but it's the

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1 mechanism, regulatory mechanism that should make it
2 very efficient for licensees to use it.

3 CHAIRMAN MALMUD: It sounds as if we have
4 two possible mechanisms. One is the NRC Commentary
5 11. The other one is, as you mentioned, the planned
6 special exposure, which would be contemporaneous or in
7 anticipation of it.

8 The next question was from Dr. Williamson.

9 MEMBER WILLIAMSON: Yes. Just a couple of
10 comments. As I noted earlier today, I was not given
11 the opportunity to study the Commissioner's voting
12 record nor the written response that was made to our
13 report, but in scanning it, I would point out a couple
14 of recommendations, technical recommendations that
15 seem to, you know, not have been responded to
16 directly.

17 One was that the issue of shielding not
18 being used or being used and whether the dwell time of
19 the patient was 39 or 77 hours. Based on the
20 information we were able to get from interviews both
21 with the Region III -- was that right? -- inspectors
22 and a representative of St. Joseph's Hospital, it is
23 not so clear cut, you know, who was right. There is
24 evidence that a reasonably thorough reconstruction
25 more contemporaneous than the interviews by the

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1 inspectors was done, and I think the recommendation
2 was clearly made by us that when there is a
3 controversy like this between the reconstruction of
4 the licensee and the inspectors, that you know, I
5 think a good faith effort should be made in the
6 inspection reports to document the bases of the two
7 calculations, and if NRC chooses to ignore the
8 licensee's reconstruction or disagrees with it, he can
9 state why.

10 Because there was contradictory
11 information available to us as to, in fact, how
12 thorough the Region III interviews and reconstruction
13 were, and I think that it seems like sort of a little
14 bit of a not whitewash exactly, but anyway, we put a
15 significant effort in trying to explore this technical
16 point, and we did make a general recommendation, which
17 was to use these additional pieces of information to
18 try to bracket the number and realize that there is an
19 uncertainty.

20 We, of course, recognize in this case that
21 their reason for interest in it was largely political
22 in the sense that someone outside the agency had
23 chosen to make an example of this, but you know, one
24 could imagine scenarios where the interval of
25 uncertainty could include a regulatory limit and, you

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1 know, an enforcement action might rely on some of
2 these distinctions.

3 So you know, while in this case we all
4 know that the regulatory limit was 100 MR and well
5 below anybody's reconstruction, nonetheless we were
6 asked to come up with feedback to inform your process
7 and, you know, make it more robust and to have higher
8 scientific credibility in the future, and so this was
9 one of our recommendations.

10 When, you know, there is a hint of
11 controversy and, you know, a reasonable alternative
12 basis for reconstructing, you know, outline it in your
13 report and give the reasons, you know, for rejecting
14 one rather than stating an interval.

15 I think the second is that, you know, I
16 glanced through the rationale for while computational
17 methods should be rejected. I don't find it very
18 convincing. I think that in a situation like this
19 where there really was not adequate information
20 recorded to determine the exact position of the
21 patient, a computational methodology is a very useful
22 supplement to a purely empirical one to give you a
23 feel for how plausible it is.

24 And I think as near as I can tell from Dr.
25 Sherbini's report -- I assume it's his -- this

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1 subtlety was not brought forth from our report. We
2 did not recommend a similar computational methodology
3 to Marcus and Siegel. We suggested that more
4 sophisticated computational methodology was a good
5 supplement to a purely empirical one.

6 We did not advocate throwing away the
7 empirical one. If you recall, we stated an interval
8 which took into account essentially, you know, of
9 which one extreme was the NRC interpretation. So I
10 wanted to correct what I perceive to be a misstatement
11 and misunderstanding of our technical recommendations
12 to us, which was in a situation where it really
13 matters -- in this one I don't think it did, but
14 others conceivably in the future it could -- I think
15 it is a useful too to do computations base upon a
16 source based methodology. You can, you know, assume
17 different scenarios of distributions and so forth, and
18 that will give you a feel for how uncertain the
19 estimate is and how much it creates uncertain
20 assumptions.

21 And this is very good for giving you an
22 overall sense of how much confidence to place in a
23 purely empirical approach, which is as arbitrary as
24 any other, I will add, and I think has no more basis,
25 you know, in fact than any of these others. They're

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1 all based on a lot of suppositions for which there is
2 no direct way of verifying. All you can do is look at
3 a range of plausible scenarios and say it's somewhere
4 in this interval is where the truth is, and that would
5 be, I think, the scientific approach.

6 This is costly, and so you don't want to
7 have to do this in every case, but I think, you know,
8 one can use one's judgment, and you know when it's
9 close to a regulatory limit and when it matters and
10 when it doesn't.

11 CHAIRMAN MALMUD: Thank you, Dr.
12 Williamson.

13 So in conclusion, Dr. Sherbini, Dr.
14 Williamson, the other interested parties, I think that
15 your slides summarize it well under your conclusions,
16 your outcomes, planned actions, that some positive
17 action will come out of the controversy that
18 surrounded this particular case, and that the existing
19 documents, meaning the NCRP Commentary 11 and the
20 special exposure possibility will allow for this to be
21 dealt with in a less controversial fashion in the
22 future, with better outcomes for all of those involved
23 via the regulation as well as family of caregivers who
24 might be involved.

25 And thank you for the presentation. Thank

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1 you, members of the committee, for you comments.

2 Mr. ESSIG.

3 MR. ESSIG: Just one final comment if I
4 may. Just as a heads up to the committee, we will
5 probably be engaging you in the future as we attempt
6 to flesh out the issue of guidance for effective dose
7 equivalent, external effective dose equivalent. The
8 Commission has directed us to come up with something,
9 some guidance which we interpret to mean beyond -- we
10 had a regulatory issue summary which we issued, which
11 was issued last year, 2003-04, and it specifically
12 addressed the issue of the use of effective dose
13 equivalent when computing doses of this type.

14 That was an issue that was raised by Drs.
15 Marcus and Siegel in their critique, and so we asked
16 the Commission, well, was the risk not sufficient for
17 the medical community.

18 And so we've been asked to engage with the
19 stakeholders in the medical community, and we will
20 probably use this committee as a vehicle for that
21 engagement, and that is the question will become then
22 what beyond the guidance that was in that regulatory
23 issue summary that I mentioned is needed to
24 effectively use the quantity or the term, the concept
25 effective dose equivalent as applied to a member of

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1 the public in a medical setting.

2 So I'm just letting you know that we will
3 be coming back to the committee with that engagement
4 in the future.

5 CHAIRMAN MALMUD: I'm certain that I speak
6 for the members of the committee who from their past
7 enthusiastic participation in this process would
8 welcome the opportunity to work with the staff of the
9 NRC in developing such a policy regarding effective
10 dose equivalent.

11 And thank you, again, Dr. Sherbini.

12 And may we move on to the next item on the
13 agenda as we are slightly behind our schedule?

14 MR. ESSIG: Yes, and I have the next item,
15 and what we propose to do is to cover this, rather
16 than the hour that's allocated, we would propose to
17 cover it in 25 minutes, and that would get us right
18 back on schedule then to hear Dr. Zelac at 4:15.

19 And the medical event item on the agenda
20 was one that we put there. We have made comments in
21 the past about the need to engage the committee in the
22 review of medical events in the future. You now have
23 access to the NMED database, and so what I'd like to
24 do is just kind of walk through some introductory
25 points and then we'll have some abbreviated

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1 presentations we'll follow with.

2 This item has been added to the agenda,
3 and you'll see it on the committee's agenda every
4 meeting. We're going to try to cover medical events
5 at every meeting. It supports Commission direction to
6 review medical events for possible trends and apparent
7 root causes and provide feedback to us, and of course,
8 we desire to gain whatever additional insights we can
9 from the committee's wisdom.

10 And so the focus will be on the evaluation
11 of medical events, will be to identify any long-term
12 trends, to identify implementation impacts, that is,
13 are there regulatory obstacles that may have been, in
14 part, the cause of the event; to identify needed
15 changes to the medical program as the result of
16 feedback from events.

17 Now, the outcome that we desire is to gain
18 the committee's feedback on trends and root causes of
19 repetitive events over the long term, any insights
20 that the staff may use to address the occurrence of
21 repetitive events, recommendations staff may share
22 with licensees to enable them to reduce medical
23 events, and insights on says that the staff may
24 interact with industry to enlighten them on what they
25 can do to reduce medical events involving devices.

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1 So the framework for the interactions on
2 this what is to become a standing agenda item is that
3 you will be provided a printout of all medical events
4 for review in the briefing binder. That will be
5 express mailed to you. We will make presentations on
6 those issues and medical events in which we are
7 looking for specific feedback from the committee.

8 The committee will then be asked to
9 provide coordinated comments on the package of events
10 and focused on the outcomes that I just mentioned.
11 The length and the breadth of the discussion will be
12 driven by the type, frequency and nature of the
13 medical events in the regulating community.

14 If there are no pressing issues to discuss
15 by either the NRC or the committee, no significant
16 time will be devoted to this agenda item during a
17 given ACMUI meeting.

18 And the topics that we would like to
19 discuss today had we taken the full agenda, there are
20 four categories there that I believe are in your
21 package: incorrect dosage administration of Sumerian
22 153, Strontium 189, and I-131, biannual brachytherapy
23 medical events, medical device registration concerns,
24 and medical events involving a Novoste device.

25 And so what I'd like to do is to have an

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1 abbreviated presentation and if, Linda Gersey, if you
2 could run through yours in an abbreviated fashion and
3 then followed by Donna-Beth Howe, and she'll run
4 through her presentation in an abbreviated fashion,
5 and that may enable us to get back on schedule.

6 MS. GERSEY: Actually everyone does have
7 a handout, and you should have a revised handout that
8 was given to you this morning, and we actually updated
9 the events to include all of fiscal year 2004.

10 Actually I won't go over the first part of
11 my handout. If you'd like to turn to the slide that
12 says "NRC Concerns One" at the top, this should be on
13 page 3. I'm going to skip all of the first part.

14 The summary is there were 35 medical
15 events for fiscal year '04, and I won't go through
16 those. You actually have handouts of every single
17 event in your binders.

18 So let's look at the first concern. We've
19 noticed that there's kind of a small trend, as you
20 might say, regarding diagnostic procedures where
21 patients are given therapeutic doses instead of the
22 diagnostic doses.

23 Specifically, there were five I-131
24 medical events in fiscal year '04. Each of these
25 events involved patients receiving therapeutic doses

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1 of Iodine 131 instead of the diagnostic doses that
2 were prescribed.

3 We thought that was quite a high number,
4 five of them within a fiscal year. In fiscal year
5 '03, there were actually four events, very similar,
6 exactly the same thing.

7 All of these events had underlying causes.
8 The first one was failure to follow procedures to
9 verify the dose or lack of procedures to actually
10 verify the dose, human error basically in these
11 instances.

12 The second part of that -- yes?

13 MEMBER WILLIAMSON: Verification of dose
14 would have consisted of comparing what they thought
15 the prescription was against a policy or --

16 MS. GERSEY: Yes. That or actually
17 looking at the label when it came in with the iodine
18 capsule, you know, any of that, just verifying what
19 they're giving the patient, any type of verification
20 that could be anywhere in the process.

21 Part of that also was not recognizing that
22 larger doses that were given required a written
23 directive. As we all know, anything greater than 30
24 microcuries of I-131 require written directive. So
25 the technicians, technologists that were administering

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1 these doses didn't even recognize, gee, if it said
2 three millicuries. It didn't even tip them off maybe
3 that there's an issue here with that, that they don't
4 realize.

5 You know, usually when there's a written
6 directive, people are more involved with paper work
7 and that kind of thing, whereas the technologists
8 didn't in this case. They just gave it to them. Part
9 of that, obviously, is not verifying the dose.

10 So in this instance we've asked the
11 committee to help us to think about some ways that the
12 NRC could communicate to licensees anything that would
13 help them prevent these type of events. For example,
14 any best practices or any suggested ways of dealing
15 with training; for example, specific things that will
16 really help someone identify something for the
17 technologists when they're actually giving the doses.

18 So what we would like to ask the committee
19 to do, and specifically Dr. Malmud, to maybe designate
20 someone to think about these thing. You have the
21 events in your binders. Review the events, those five
22 specific I-131 events, and try to come up with some
23 maybe best practices or something that we could
24 communicate to our licensees. Can't think of anything
25 specific? Well, that's an okay answer, too, because,

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1 you know, we're not sure how to communicate that as
2 well.

3 Yes, Dr. Williamson.

4 MEMBER WILLIAMSON: Do you think this is
5 a rising trend or is it the same?

6 MS. GERSEY: Well, like I said, in fiscal
7 year '03, we had four events. This year we had five.
8 But it seems like it should be preventable.

9 MEMBER WILLIAMSON: What's the
10 denominator?

11 MS. GERSEY: I absolutely don't know.

12 MEMBER WILLIAMSON: I really think it
13 would be good because I know even back as long ago as
14 1995, there were estimates of denominators, and it
15 would be useful to know.

16 MS. GERSEY: Yes, and unfortunately I
17 don't have those with me today.

18 CHAIRMAN MALMUD: In this case I think the
19 denominator doesn't matter. We should be heading to
20 zero error. So that we will respond to your request.

21 MS. GERSEY: Okay.

22 CHAIRMAN MALMUD: Because clearly a
23 patient who should have gotten ten millicuries and got
24 100 millicuries received a radiation burden which was
25 unnecessary.

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1 MS. GERSEY: Right.

2 CHAIRMAN MALMUD: And with doses of that
3 magnitude, we head for zero. We aim for zero error,
4 and we will regard it as something which should be
5 heading towards zero error.

6 Dr. Eggli.

7 MEMBER EGGLI: I would agree that the
8 error on therapeutic doses should approach zero.
9 However, I think it is useful to understand the
10 magnitude. In my practice alone, we administer over
11 1,000 doses of radioactive iodine above one millicurie
12 every year.

13 MEMBER WILLIAMSON: I didn't mean my
14 comment to suggest that trying to drive it down to
15 zero is not a worthy effort. It is, but I think that
16 any conclusions about whether it's caused by a change
17 in the regulatory system and so forth should be
18 accompanied by a statistical analysis to determine
19 whether there is a significant --

20 MS. GERSEY: And I don't think that's the
21 goal of --

22 CHAIRMAN MALMUD: No, I wasn't suggesting
23 that you were minimizing it. It just doesn't matter
24 what the incidence is. We still have to work on the
25 issue.

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1 MEMBER WILLIAMSON: But when a policy
2 decision, you know, or critiquing a regulatory
3 approach, then you should really, I think, present the
4 denominator.

5 CHAIRMAN MALMUD: Sure.

6 MEMBER WILLIAMSON: And consider the
7 statistical sampling issues.

8 CHAIRMAN MALMUD: But if I may, I'll
9 appoint the committee to work on the problem while
10 we're still getting the data with regard to the
11 denominator.

12 MS. GERSEY: Thank you, Dr. Malmud.

13 Okay. If we can go on to the next item,
14 which is NRC concern number two, this is in regard to
15 medical devices, certain medical devices that are
16 actually not reviewed for sealed source and device
17 registry by the NRC.

18 As you hear from Dr. Jankovich this
19 morning, he talked all about the SS&D program. There
20 are certain types of medical devices that, of course,
21 are always reviewed by the FDA for medical use in
22 humans, but there are some devices after being
23 reviewed by the FDA are not reviewed for radiation
24 safety issues by the NRC, and I'm going to give you
25 two examples.

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1 The first one is the MICK applicator for
2 brachytherapy seeds. That has never received a sole
3 source and device review by the NRC. It has been a
4 policy of the NRC not to review these devices.

5 The question here is should NRC change
6 their policy and actually review these. The question
7 about this is we do know that for the MICK applicator
8 there have been two related events, reportable events,
9 in 2004. There have been two related events in 2003.
10 We also had some events that have happened and are not
11 reportable. They don't fall under the criteria of
12 reportable in the NRC regulations, but events that
13 have occurred being used when the MICK applicator is
14 actually being used.

15 So, for example, a seed is sheered or the
16 applicator gets stuck with the seed in it, and I think
17 that we understand this.

18 Dr. Williamson?

19 MEMBER WILLIAMSON: Here's the situation
20 where I do think the denominator, which is
21 approximately 50 to 60,000 cases a year, is relevant
22 because now you're contemplating basing a policy
23 decision on two incidents. So we should really, you
24 know, think about of course it's regrettable that even
25 one incident occurs, but you have to balance this

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1 against the fact that these are very small companies
2 that can produce these devices. They're very valuable
3 for many patients, and the size of the burden you
4 create in contemplating, you know, additional scrutiny
5 must be considered.

6 MEMBER NAG: I think here I can give my
7 personal experience. I have been using the MICK
8 applicator for many, many years. The MICK applicator
9 itself is not a radioactive device. You are using
10 radioactive material that you're loading into it
11 afterwards. I mean, in that situation you should be
12 then filling up the syringes because you are putting
13 radioactive material inside the syringe.

14 So is NRC going to review every syringe
15 manufacturer in the world? No.

16 My personal opinion, the MICK applicator
17 itself is not radioactive. It is a method to put the
18 radioactive materials into the patient, and therefore,
19 the MICK applicator itself is not within your
20 jurisdiction.

21 MS. GERSEY: Thanks for that comment.

22 Actually I would like to ask Dr. Vetter
23 because he mentioned the MICK applicator this morning
24 and the fact that seeds can get sheered. I'd like to
25 know what your opinion is about that.

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1 And you can think about it and get back to
2 us if you can't think of --

3 MEMBER VETTER: Well, regardless of
4 jurisdiction, I would agree with Dr. Nag that it's not
5 the applicator. It's the user. There's something
6 wrong. I mean, they're in a hurry. They're doing a
7 lot of these. They punching 100 seeds into this
8 prostate or how many that day?

9 Okay. Sometimes it doesn't work quite as
10 smoothly as it does other times, and this one time,
11 you know, you push a little hard, and you sheer the
12 seed. But the applicator itself I don't think was the
13 problem.

14 CHAIRMAN MALMUD: Yes, Dr. Miller.

15 MR. MILLER: If I could offer a thought
16 based upon what I hear from the committee comments,
17 the question as Linda phrased it was: should NRC
18 change a policy and require SSND reviews for these
19 types of medical devices?

20 I think I heard from at least some
21 committee members the answer to that question as being
22 no. So I guess the question that I would ask is does
23 this require further study on the part of the
24 committee or do you think that you're prepared today
25 to make a recommendation?

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1 I think that's what you're looking for.

2 MS. GERSEY: Yes.

3 MR. MILLER: A recommendation.

4 MS. GERSEY: Sure, if you can do that
5 today.

6 MR. MILLER: I'm not trying to push you to
7 do that, I mean, but it sounded like from a couple
8 committee members' comments you felt it was an open
9 and shut kind of case, unless I misinterpreted what
10 Dr. Williamson and Dr. Nag said.

11 MS. GERSEY: I'm just going to interject
12 here as well. I did have one other example of a
13 medical device that has not been reviewed by the NRC.
14 If you don't mind, I'll just briefly tell you what
15 that is.

16 There is a company that is imbedding
17 brachytherapy seeds into suture material. They're
18 melting the suture material, and they're putting the
19 brachytherapy seeds in, and a part of the procedure
20 which actually you heard Dr. Jankovich this morning
21 talk about is they are cutting the suture material
22 into the size that they need, and it is the potential
23 for cutting the seed and can cause leakage and so
24 forth.

25 That type of thing has not been evaluated

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1 by the NRC, and it's another example of something that
2 we haven't done.

3 CHAIRMAN MALMUD: Okay. Dr. Vetter.

4 MEMBER VETTER: I guess it's my opinion
5 that both of those are user errors, and perhaps it
6 should be handled in a manner similar to the I-131.
7 Determine what it is that's being done. Are they in
8 too big a hurry? What's being done wrong? And try
9 and communicate some advice to the users.

10 MS. GERSEY: And actually it is the device
11 distributor who's actually making these and giving it
12 to a licensee. So it's not the end user so much but
13 actually it's part of the company. They get the seeds
14 in, and they make these strands, and then they
15 distribute them.

16 MEMBER VETTER: I know. We cut them. We
17 use them, and we cut them. We don't have the seeds,
18 but --

19 MS. GERSEY: No, actually it's actually
20 the distributor who cuts them.

21 MEMBER VETTER: And in this case?

22 MS. GERSEY: In this case, yes.

23 MEMBER VETTER: And they cut one of the
24 seeds?

25 MS. GERSEY: They have in the past, yes.

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1 MS. Schwarz: After they cut them do they
2 distribute them?

3 MS. GERSEY: Well, yes, but we don't 100
4 percent know whether or not it's --

5 CHAIRMAN MALMUD: Dr. Nag?

6 MEMBER NAG: Can I just add to that? I
7 think you are talking about the rapid (phonetic)
8 strand.

9 MS. GERSEY: Yes.

10 MEMBER NAG: Is that? Okay. The rapid
11 strand is --

12 MS. GERSEY: No, actually the ready
13 strand. The ready strand?

14 MEMBER NAG: Okay.

15 MS. GERSEY: Is that okay?

16 MEMBER NAG: That's similar to the rapid?

17 MS. GERSEY: Yes.

18 MEMBER NAG: Is it in a white material or
19 is it in a hardened material?

20 MS. GERSEY: It's in a suture material,
21 long strand of --

22 MEMBER NAG: All right. So basically what
23 is happening, you're having seeds that have been put
24 into sutures. Basically it has to be an up rate
25 error, whether they up rate the end user or the

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1 distributor. You are supposed to look at the seeds,
2 and there is a half centimeters spacing between the
3 seeds.

4 So when you're acting, you have to see
5 that you're you're acting within the seed. This is
6 the same thing as iridium that comes in a ribbon.
7 When you cut them, if you cut them, you are always
8 supposed to look at the iridium ribbon and cut in
9 between the ribbon. This is not something in the NRC.
10 It is in whoever is cutting it, whether the end user
11 or the distributor. This is just simple common sense.

12 DR. HOWE: Dr. Nag, this is Dr. Howe.
13 What is happening for the ready strand is that they
14 are not cutting in the space of material between
15 seeds. They're actually trimming the side of the
16 melted plastic to insure that it will fit into a
17 syringe, and as they are trimming that excess material
18 off, there's a high probability of nicking, and we've
19 had two medical events within a month.

20 MEMBER NAG: That is a different question
21 than the rapid strand. I mean, that really will
22 require further thought, but in terms of the MICK
23 applicator, the MICK applicator itself is non-
24 radioactive. You know, whether you are using
25 radioactive seeds or any other seed, you are

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1 introducing something from the outside.

2 So I don't think the MICK applicator is
3 anything that we need to worry about.

4 In terms of the rapid strand, I don't
5 think it's something we have to worry about, but in
6 terms of the new one, I think I have to think a little
7 bit more and look into what exactly the manufacturer
8 is doing before I can give my opinion.

9 MEMBER DIAMOND: It would seem in that
10 particular instance that's a manufacturing issue, and
11 that that technique lends itself to an unacceptably
12 high risk that you could go and penetrate these seeds
13 as you're trying to trim it.

14 That's human error. You're talking about
15 trying to go get these very narrow diameter bical
16 (phonetic) seeds, seed trains within a set of needles.
17 They should really look at how they do their
18 manufacturing to see if they can go to eliminate the
19 need for manual trimming.

20 CHAIRMAN MALMUD: Dr. Williamson.

21 MEMBER WILLIAMSON: Well, one general
22 point is if you were contemplating, you know, just in
23 general, this could potentially be a vast expansion,
24 you know, of your regulatory activities to start
25 thinking about, you know, all of these different

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1 ancillary devices that are used in brachytherapy:
2 buttons, needles, catheters of all different kinds,
3 obturators of all different kinds.

4 I really think you should rather than be
5 driven by a specific example, as Dr. Siegel used to
6 call it, the yo-yo method of regulation basing a
7 policy shift on, you know, a tiny statistical sample
8 of events, you know, think through and really have
9 some good criteria about when, you know, an
10 intervention or change in policy is needed.

11 So I would say, first of all, develop
12 then a general approach of deciding when you're going
13 to take on one of these many devices and what
14 constitutes an acceptable risk or non-negligible
15 number of events.

16 You know, specifically with regard to this
17 seed stand operation, you know, one question I would
18 ask is whether you have had, you know, adequate
19 regulatory authority between NRC and FDA to handle
20 this. I should think that in a manufacturing
21 operation, if somebody violates the integrity of one
22 of their seeds and sends it out, the best way to
23 handle it is for somebody to cite them for a violation
24 either of good manufacturing practices or of their
25 license conditions, and they will no doubt be disposed

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1 then to correct their behavior and improve their
2 manufacturing standards so that this is minimized.

3 So rather than, you know, creating a
4 separate regulatory apparatus, I would ask you if you
5 have exhausted other regulatory approaches to handling
6 this matter.

7 MEMBER SULEIMAN: This sounds like a
8 medical device today.

9 DR. HOWE: Yes, it is.

10 MEMBER SULEIMAN: Are you aware of
11 anything about this specific product? Get me the
12 information and we'll do what we can.

13 DR. HOWE: Yes. We're currently talking
14 with FDA, Office of Compliance for the medical devices
15 to see if they have an interest in following up on
16 their end of it, and we're taking inspection
17 enforcement action.

18 MS. GERSEY: Thank you.

19 CHAIRMAN MALMUD: Does that complete your
20 --

21 MS. GERSEY: That certainly does.

22 CHAIRMAN MALMUD: May I indicate that Dr.
23 Eggli, Schwarz, and Vetter have agreed to be the
24 subcommittee to deal with the nuclear medicine issue.
25 Dr. Eggli will chair the committee, and that will deal

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1 with the radioiodine doses.

2 For the radiation therapy issues, I would
3 ask those who already have a heavy burden to jump in
4 on this one. Dr. Diamond, as a radiotherapist, would
5 you be interested in this particular --

6 MEMBER DIAMOND: Exactly what is my
7 charge?

8 CHAIRMAN MALMUD: Your charge is to take
9 a look at the items in this agenda item that have to
10 do with radiotherapy misadministrations or incorrect
11 doses to see if you can apply policy changes or
12 recommendations that might help prevent these kinds of
13 problems from recurring.

14 Some of them are human error and can't be
15 except perhaps --

16 MEMBER DIAMOND: So is there a root cause
17 and if so any methods to correct that root cause --

18 CHAIRMAN MALMUD: Correct.

19 MEMBER DIAMOND: -- that is within our
20 purview?

21 CHAIRMAN MALMUD: Correct. And asking to
22 work with you would be a physicist who does radiation
23 therapy.

24 (Laughter.)

25 CHAIRMAN MALMUD: And to round out a

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1 committee of three, may I ask Dr. Nag, who I have
2 already asked to do two other things today as a
3 therapist.

4 Thank you.

5 MEMBER DIAMOND: That was a yes, for the
6 record, from Dr. Nag.

7 (Laughter.)

8 CHAIRMAN MALMUD: That covers, I believe,
9 the two classes of problems you have presented to us.

10 The third one which has to do with non-
11 radiation devices which are used is really more, as I
12 see it, more in the realm of the FDA, and I don't know
13 that we are the correct body to get involved in that,
14 and I would leave the wisdom of that to Dr. Suleiman
15 if he has a recommendation as to how we might approach
16 this or not approach it.

17 MEMBER SULEIMAN: Well, I'll follow up,
18 but clearly if you've already been talking with some
19 of our people, I need to find out who you're talking
20 to and what the status is, but clearly this sounds
21 like a straightforward issue.

22 CHAIRMAN MALMUD: Very good. Does that
23 address the issues that you wanted to?

24 MS. GERSEY: Yes, it does. Thank you very
25 much.

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1 CHAIRMAN MALMUD: And we have our
2 subcommittees designated.

3 Thank you.

4 And what will the time frame be? How
5 urgent is this issue for you?

6 MS. GERSEY: Actually I had suggested
7 maybe two months.

8 CHAIRMAN MALMUD: Two months acceptable?

9 MS. GERSEY: That any recommendations we
10 would evaluate and the next ACMUI meeting we would
11 tell you how we processed those.

12 CHAIRMAN MALMUD: Okay. I believe, Dr.
13 Diamond, is that okay?

14 MEMBER DIAMOND: That's fine.

15 MS. GERSEY: thank you.

16 MS. GERSEY: Thank you.

17 MEMBER EGGLI: Do these evaluations come
18 back to the whole ACMUI committee or just staff?

19 CHAIRMAN MALMUD: It's a subcommittee
20 report. So it would come to the chairman of the
21 committee.

22 MEMBER EGGLI: Okay.

23 CHAIRMAN MALMUD: And then we'll review it
24 as a committee and present it to NRC staff for its
25 review. Is that the correct process?

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1 MS. GERSEY: Yes.

2 CHAIRMAN MALMUD: That's the one we'll
3 follow.

4 MS. GERSEY: Great. Thank you very much.

5 MEMBER LIETO: Okay, and then Dr. Howe
6 will make an abbreviated presentation.

7 CHAIRMAN MALMUD: Oh, I'm sorry.

8 MEMBER LIETO: That's all right.

9 CHAIRMAN MALMUD: I didn't mean to ignore
10 you.

11 MEMBER LIETO: Yeah. Well, I couldn't let
12 you go twice.

13 What we're doing right now, is this just
14 having to do with the specific instances that Linda
15 has just brought up?

16 CHAIRMAN MALMUD: Yes.

17 MEMBER LIETO: Okay. So what Donna-Beth
18 is going to talk about is the database in general, and
19 we're going to address those issues?

20 CHAIRMAN MALMUD: We're looking at those
21 specific issues and wondering if from our perspective
22 there's a recommendation that we could make that would
23 prevent these kinds of errors from recurring,
24 recognizing that some are just human errors even with
25 multiple controls and in other instances there may be

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1 some additional controls or recommendations which
2 could be applied across the board.

3 Does that answer your question? You still
4 look --

5 MEMBER LIETO: No, just perplexed, but
6 I'll wait until I hear Donna-Beth's presentation, and
7 then if I still have questions, I'll come back.

8 CHAIRMAN MALMUD: Okay. Dr. Nag has
9 another point?

10 MEMBER NAG: Yes. Does it include all of
11 these medical plans in here?

12 CHAIRMAN MALMUD: Only those related to
13 radiotherapy for you and only those related to
14 radioiodine for Dr. Eggli.

15 MEMBER NAG: Okay.

16 CHAIRMAN MALMUD: Dr. Howe.

17 DR. HOWE: What I'd like to do is bring
18 you up to date. We've been monitoring intervascular
19 brachytherapy and the Novoste product because we've
20 had more medical events and more product failures and
21 event reports that are beyond the Part 35 scope with
22 Novoste than we've had with any other devices.

23 And it's important for me to point out
24 that the Novoste device is an ever evolving device,
25 and so the company is continually making engineering

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1 and mechanical changes to the device, and so our
2 review of events and medical events to some extent
3 shows the progression of that evolution.

4 If you looked at my slides, I had a
5 summary slide that told you of the medical events, and
6 they were 35, and I broke them down by categories and
7 those are the ones you have in your paper. And I just
8 wanted to focus on the IBBs, which are the five at the
9 bottom that are resulting from 35-1,000 use.

10 And what I've also done is not only is it
11 important to look at the medical events at Novoste,
12 but also to look at the events that are coming in
13 under Part 20 or Part 30, and so we've had two events
14 that really have nothing to do with the device, and
15 that is the licensee's lost their devices. Okay? You
16 would think they would have better inventory for this
17 device, but that being said.

18 When we get to the other two events and
19 then the medical events, what you see is a common
20 thread. First of all, during this year, there were
21 almost no five French devices. So the year before
22 there were 16 events involving Novoste. In FY 2004,
23 there were nine events. You're not seeing the five
24 French events anymore. You're not seeing the sources
25 separating because now they're in a jacketed source

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1 train.

2 What we're seeing primarily is kinking.
3 We're seeing the catheter kinking at the distal end
4 due to torturous anatomy. We're seeing it at the
5 proximal end possibly due to how the device is being
6 held, whether it's being held parallel to the catheter
7 or more perpendicular.

8 We're also seeing kinking from clamps that
9 are either tightened too tight. We had been told by
10 the manufacturer that the Tuohy valve problem had
11 pretty much disappeared. We're still seeing at least
12 one of that that's a result of the Tuohy valve.

13 And we're also seeing events where they
14 haven't opened the valve totally, and it appears as if
15 the authorized user is not using the fluoroscopy to
16 really see where the device is, and they're using
17 other things like fluid flow. And fluid flow is not
18 a good indication that the device is working properly
19 because we've had a number in here where the fluid
20 flow they comment was perfect, and it wasn't until the
21 next day they discover the sources never got to the
22 area.

23 There's also beginning to see that with
24 the 3.t French the sources in the markers, the distal
25 and proximal, they're pretty small, and it's difficult

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1 sometimes on fluoroscopy to see and to interpret
2 what's being looked at, and we've had a number of
3 cases where the user has indicated that they use
4 fluoroscopy to confirm where the sources are, and then
5 the next day they discovered that the sources weren't
6 anywhere near the treatment site.

7 So the very last slide that I have pretty
8 much sums up that with the 3.5 French device what
9 we're seeing primarily is kinking. The proximal end,
10 the distal end, in the middle -- yes, Jeff.

11 MEMBER WILLIAMSON: Oh, I don't mean to
12 interrupt you in mid-sentence. I just had a question
13 to follow.

14 DR. HOWE: An over tightening of clamps
15 and valves that aren't open enough, where we're seeing
16 that the users, the authorized users are having
17 difficulty identifying things on fluoroscopy, and
18 we're also finding that they're not -- one reason
19 they're having more medical events in some of these
20 events, they knew they're hitting resistance. They
21 weren't following the manufacturer's recommended
22 guidelines that if you can't see it at the end of 15
23 seconds, you need to pull the sources back and see
24 what's wrong.

25 So those are kind of our root cause

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1 observations.

2 Jeff?

3 MEMBER WILLIAMSON: I guess I should have
4 read these more carefully. I'm having a little
5 trouble understanding whether the majority of the
6 events are due to user deviations from the established
7 practice or whether there's some inherent flaw that's
8 causing more events in the 3.5 French system.

9 I guess the reduced radiographic
10 visibility, one might consider that, I suppose, to be
11 a flaw in the newer system relative to the old, but is
12 the kinking business caused by inherently increased
13 fragility of the catheter or is it caused by maybe the
14 procedure frequency going down and users aren't as
15 expert anymore or is it caused by the fact that they
16 can push the 3.5 French catheter into smaller, more
17 tortuous vessels where they couldn't go before and
18 this is causing a larger number of events?

19 And here's where I would think a
20 denominator would really help you because we know that
21 probably the utilization of the device in absolute
22 terms is going down. So to keep an eye on relative
23 safety, it would be helpful for you to know the
24 denominator.

25 DR. HOWE: Yeah, I think the device is

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1 small enough that it can go into tighter places, and
2 so people are putting it into tighter places, and it's
3 not going. It's a little bit too fragile to get
4 there, and so it's important to understand its
5 limitations. And that's one area.

6 I think the manufacturer is working on and
7 trying to prove the fragility of the device and try to
8 make it a little bit more robust on the end so that it
9 doesn't twist.

10 CHAIRMAN MALMUD: I think Dr. Nag had a
11 comment.

12 MEMBER NAG: Yeah, yeah. One other thing
13 you have to realize is that the other two
14 manufacturers in intervascular brachytherapy have now
15 gotten out of the market, which means people who were
16 previously used to using P-32 and iridium can no
17 longer use them for intervascular brachytherapy, and
18 that when they had to switch over to the Novoste
19 whether they liked it or not, Novoste now is the only
20 approved brachytherapy, interventional brachytherapy
21 device in the market.

22 So you are having a number of people who
23 although they have done interventionally brachytherapy
24 before and think they know all about that are now
25 going into a new device which operates entirely

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1 differently, and that does create a new level of
2 difficulty because they think they know all about
3 that, and they don't need any special training, and
4 now they're going ahead and finding it different.

5 So I think there is that element, and the
6 second element is that because this is now a narrower
7 catheter, we are now trying to go in through the
8 distal artery that we were not doing before, but we
9 were doing that with the P-32 device.

10 CHAIRMAN MALMUD: Thank you.

11 DR. HOWE: And I think we see more medical
12 events when they fail to retract in 15 seconds. You
13 see in here there's one medical event where the
14 cardiologist started to stop to discuss with the
15 oncologist, but left the sources in the wrong place
16 for over two minutes.

17 And then another one where they realized
18 it wasn't in the right source, but it took them 47
19 seconds to pull it out, and then they tried again, and
20 then they left it there for ten seconds.

21 So you're having a combination between the
22 device itself and the users not necessarily being as
23 sensitive to the fact that they are going to have to
24 be careful when they're using it and really observe
25 things carefully.

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1 CHAIRMAN MALMUD: Dr. Nag.

2 MEMBER NAG: Another practical problem
3 that does occur in practice is that the cardiologists
4 are putting the catheters in. The radiation
5 oncologist is not there at that moment when they're
6 putting the catheter in, and once they have done their
7 job, opened up the blockage, then they call the
8 radiation oncologist, and appoint the radiation
9 oncologist, who may be in the middle of five other
10 things, and by the time they come, they are then
11 rushed and say, "Oh, okay. Go ahead. You know, go
12 ahead and put that in."

13 So you have to then have a tug-of-war
14 that, no, I want to see where it's in, and you know,
15 it's like, "Go ahead and push it in." You know, those
16 things go on in practice.

17 CHAIRMAN MALMUD: Thank you for your
18 observation. Is that --

19 MEMBER DIAMOND: Just one other comment.
20 Number one, just for the benefit of the audience, it's
21 important to recognize how much this field has
22 constricted in the past year. My particular center
23 was the second busiest center in the country doing
24 this two years ago. I think the last time I did a
25 vascular brachytherapy procedure now was probably six

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1 months ago. It has been really completely replaced by
2 the coded stents.

3 Some of it may be due to improved
4 efficacy, although I'm not sure about that. Certainly
5 a lot of it has to do with the economic forces.

6 The next part of that is I still believe
7 that the great majority of these events are due to
8 either operator error or inexperience in that we're
9 going after the smallest, highest risk vessels. These
10 catheters by their small size are naturally fragile.
11 There's a lot of manipulation involved, and the simple
12 point is you can't expect even in the best of
13 circumstances for any catheter to be kink free, and if
14 you simply recognize during your initial run that
15 there's a kink, you know that that's a patient with
16 that particular catheter in place; you can't deliver
17 the treatment.

18 And most of these errors drive from
19 physicians trying to do treatments where it's just
20 physically not capable of being accomplished, and if
21 you just realize that and say either we can't do it to
22 this patient because of the anatomy of the vessel, or
23 if we want to try it, pull out this catheter and try
24 it again with a different one.

25 I think that's the great bulk of the

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1 issue, is operator experience or unrealistic
2 expectations.

3 Thank you.

4 CHAIRMAN MALMUD: Thank you.

5 Thank you, Dr. Howe.

6 Back to our agenda. There's a question
7 from --

8 MEMBER LIETO: Yeah, back to the medical
9 event. A couple of comments that I'd like to make.
10 One is that the NMED that we're talking about, we're
11 looking at sort of like maybe two subsets of medical
12 events. I mean of events that relate to medical use.
13 If you look at the NMED database, there's actually ten
14 categories, and there could be events in these other
15 categories related to medical use.

16 Transportation, in other words,
17 radioactive packages coming in highly contaminated
18 which I believe there have been reportable events on
19 that. I'm trying to find what the other categories
20 are here that might be related to this.

21 But anyhow, there's other areas in the
22 NMED database that might relate to the medical use and
23 events that are not necessarily the administration of
24 a radiopharmaceutical or a radionuclide, and it would
25 be kind of interesting to see what kind of events

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1 relate to that and if those numbers are increasing.

2 I've been seeing some of these come across
3 individually on listservers and things of that nature,
4 and it seems like there has been an increase in the
5 number of radioactively contaminated packages coming
6 into facilities that used radioactive materials or for
7 the medical use of radioactive materials. So I guess
8 my question or comment to the staff, to the NRC staff
9 is: is there a way that we could get in these routine
10 reports events that relate to the medical use in terms
11 of events that are reported in the database that would
12 not necessarily be the patient issues only, but also
13 issues related to transportation, sealed source.

14 I mean, there are issues, I think also --
15 I think another category is lost sources or misplaced
16 sources. That would not necessarily be pepped up or
17 be included in this to any of the subcommittee groups
18 that were just identified, yet I think might be
19 informative to the advisory committee and might
20 provide the need for input from an overall standpoint.

21 And that's one of the reasons, you know,
22 that I had sent this item in earlier as being one for
23 discussion is because I think there are issues coming
24 up that are not the old misadministration definition
25 which I think that's the only thing that would fall

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1 under the NMED or the medical event category, are
2 those that actually meet the old misadministration
3 definition in its current revision or current form.

4 Yet there are other events that relate to
5 medical use that I think would be of value to this
6 committee.

7 CHAIRMAN MALMUD: Ralph, is that something
8 that would be of interest to you?

9 MEMBER LIETO: As an advisory committee,
10 I think so because I think we're seeing some increased
11 reports on these.

12 CHAIRMAN MALMUD: If Ralph could get the
13 data, would you be willing to serve on a small
14 subcommittee to look at that?

15 MEMBER LIETO: Sure.

16 MR. ESSIG: I don't see any problem with
17 that. What I would like to do is to have my NMED
18 project manager consult with her the first thing in
19 the morning and, as appropriate, have her come back
20 and answer Ralph's question directly tomorrow.

21 CHAIRMAN MALMUD: Very good. Thank you.

22 The next item on the agenda is Dr. Zelac
23 who will give us an update to medical event criteria
24 definition.

25 DR. ZELAC: Thank you, Dr. Malmud.

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1 More than an update, what I'm really doing
2 is seeking your input. We have been, first of all,
3 we, as you know, have in our current regulations
4 criteria that apply to all modalities for reporting an
5 event as a medical event. The first of these is that
6 the delivery of a dose differs from the prescribed
7 dose or the does that would have resulted from the
8 administration of the prescribed dosage by more than
9 .5 sieverts to an organ or tissue or .05 sieverts
10 effective dose equivalent.

11 And secondly, a total dose or dosage that
12 differs from the prescribed dose or dosage by 20
13 percent or more. This is what is in our regulation
14 currently.

15 At your last opportunity to address the
16 Commission, this issue came up specifically with
17 regard primarily to permanent implants for prostate,
18 and in the directions that the staff received for
19 follow-up to that meeting, we were asked or directed
20 to first provide recommendations on the
21 appropriateness of the current definition of a medical
22 event and, two, recommendations on effectively
23 communicating associated risks, if any, to the public.

24 We were also directed to confirm that
25 there was at the time the current rule was adopted and

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1 still is for each of these modalities an appropriate
2 basis for having the plus or minus dose variation
3 threshold for reporting medical events.

4 And finally, we were directed to involve
5 the advisory committee in developing these various
6 recommendations. It is not my expectation that we
7 will do everything today clearly in the amount of time
8 available. However, this is the beginning of the
9 process by which your input will be sought and
10 received and translated into something to put forth to
11 the Commission for consideration.

12 We decided it would be appropriate as a
13 starting point to see where it was that the plus or
14 minus 20 percent came from that appears in the current
15 regulation. If one looks at the previous version of
16 Part 20, for some modalities plus or minus 20 percent
17 was there and, indeed, was carried over to the current
18 version.

19 For other modalities, the variation that
20 was permitted had been plus or minus ten percent and
21 was raised to plus or minus 20 percent in the current
22 version.

23 I contacted the former Chair of the
24 advisory committee, Dr. Barry Siegel and discussed
25 this issue with him in terms of what the

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1 considerations had been of the advisory committee, as
2 well as of the Part 35 working group that crafted the
3 current version during the consideration of this
4 particular issue, since clearly changes had been made
5 from the previous version.

6 I hope that all of you had opportunity to
7 see and to look at perhaps in some detail the E-mail
8 that I included in the package, which was Dr. Siegel's
9 response and input for your use and for our use. I
10 offered this as a vehicle for initiating discussion of
11 this issue at this meeting and hope that you again
12 have had opportunity to review this for today's
13 meeting.

14 What we're going to try to do in the
15 remaining time if possible is review what it was that
16 brought us to where we are and reach some conclusions,
17 if possible, on the appropriateness of the current
18 medical event reporting criteria. We can consider it
19 on an overall basis, as Dr. Siegel has done in his
20 report or on an individual modality-by-modality basis.
21 It's your choice.

22 With that I open it up to any comments
23 that you would like to make about the recommendations.

24 CHAIRMAN MALMUD: Comments? Dr. Vetter.

25 MEMBER VETTER: I like Dr. Siegel's

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1 response, and especially relative to the ten percent
2 threshold. I think that is way too tight because of
3 variations in practice and also because of in certain
4 cases perhaps difficulties with trying to get the
5 prescription that tight.

6 And relative to the 20 percent, I like
7 that because based on the information we've been
8 receiving on medical errors and so forth, that does
9 not seem to be too restrictive. On the other hand,
10 it's adequate to capture the medical events that we've
11 been observing.

12 So I think I would pretty much agree with
13 him, although he didn't make a formal conclusion;
14 pretty much agree with him that the numbers seem to be
15 appropriate and should be applied in a general fashion
16 rather than modality by modality.

17 CHAIRMAN MALMUD: Dr. Williamson.

18 MEMBER WILLIAMSON: Well, two comments.
19 One is it all depends upon what you mean by
20 appropriate, and I think there's sort of two ways in
21 which the medical event criterion may or may not be
22 appropriate. One is you need some sort of relatively
23 arbitrary performance criterion in order which to
24 judge the effectiveness of a performance based
25 regulatory program. You need to have a relatively

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1 clear-cut criteria for determining whether what a
2 licensee is doing is reasonable or not or what a group
3 of licensees is doing.

4 And in that sense, it's most important
5 that the criterion represent events that the typical
6 professional would view as cause for concern from a
7 sort of QA adequacy point of view.

8 This is different than, you know,
9 attempting to identify wrongfully delivered treatments
10 that cause patient harm. Okay? So that gives you a
11 lot more flexibility in calibrating it if it's a sort
12 of harbinger of good or bad QA program.

13 I frankly think that, you know, in view of
14 the ACMUI during the formulation period of Part 35 was
15 to pitch that concept of medical event to you and try
16 to decouple it from the issue of patient harm.

17 Okay. Of course, the second criterion of
18 appropriateness might be that you want it to be
19 coupled with patient harm. Somehow you want to
20 find -- and I think this is the quandary you're in
21 because you're asking both things of the criterion --
22 you want to identify events that cause patient harm,
23 and you make a presumption through your various
24 redundant reporting requirements to the patient and
25 nonexistent guardians and so forth that, you know, you

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1 make the presumption that it has or might have caused
2 medical harm.

3 I think that is a very difficult issue
4 because it's not only going to depend on modality.
5 It's going to depend upon whether it's a post-op
6 treatment, in which case, you know, there's a lot of
7 latitude on the upper end before you cause
8 complications, or it's a definitive treatment where
9 you're pushing the patient to normal tissue tolerance
10 in order to get an acceptable cure rate.

11 Whether 20 percent materially harms the
12 patient really depends upon the steepness of the dose
13 response curve for the tumor and how closely spaced
14 the normal tissue response curves are to the tumor
15 response curve, and that's not only going to differ by
16 modality. It's going to differ by clinical setting,
17 tumor site, stage, et cetera, whether there has been
18 surgical debulking preceding the brachytherapy or not.

19 So I think if you try to come up with a
20 criterion, a single, you know, reasonably simple
21 criterion that, you know, is going to more accurately
22 capture events that may hurt or harm patients, I think
23 that's kind of hopeless. You know, I just don't think
24 it can realistically be done because it's too
25 complicated and depends upon too many medical factors.

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1 I think you would be better off sticking
2 with sort of QA sensitive events because there's a
3 more objective basis for deciding what they should be,
4 and you can kind of specify, you have a chance of
5 being able to specify what they should be
6 independently of all this medical complexity of the
7 individual patient.

8 CHAIRMAN MALMUD: May I interpret your
9 comments to mean that you are in agreement with the
10 position taken by Dr. Siegel in the letter that Dr.
11 Zelac attached to his presentation?

12 MEMBER WILLIAMSON: Yeah, I am. You know,
13 I could say I think the 20 percent is reasonable for
14 the former.

15 CHAIRMAN MALMUD: I think that Dr.
16 Suleiman was next.

17 MEMBER SULEIMAN: First off, I think FDA
18 is very, very concerned with the dosimetry, now with
19 more interventional therapeutics. I think the issue
20 is going to get more visibility.

21 I also think you have to differentiate
22 between diagnostic doses and therapeutic doses. To
23 quote a colleague, he says you can be off two or three
24 times using a MIRD dose calculation, diagnostic, and
25 nothing is going to happen really. You would be off

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1 by two or three times with a therapeutic does and
2 you've got a dead patient on your hand. So I think
3 that's really the gist of it.

4 The other thing I would address, my own
5 professional opinion though, I'm arguing this within
6 our agency, too. When you're talking about medical
7 therapies, I think you should focus on the organ doses
8 and stay away from what I call the homogenized metric,
9 you know, the effective dose equivalent because that
10 would mask.

11 That's okay for occupational limits and
12 for comparison of different source type radiations,
13 but in medical applications where you have a very
14 specific procedure and very set of specific organs
15 you're targeting, I think we should be very, very
16 accurate and say this is the target on it. This is
17 the prescribed dose.

18 In terms of what's good or what's bad, I
19 would really defer to the people practicing this right
20 now, and if 20 percent seems to be a good -- you have
21 to do something to keep people in check, but I think
22 if 20 percent seems to be acceptable, obviously some
23 specific procedures would have much, much more
24 accuracy and precision. Others probably would have
25 less.

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1 So I don't know whether we go on an ad hoc
2 basis or go with the 20 percent and let the system
3 evolve.

4 DR. ZELAC: May I comment?

5 CHAIRMAN MALMUD: Yes.

6 DR. ZELAC: First, the question does not
7 involve replacing the current dose, absolute values of
8 dose that are delivered, that 50 rem. That's not on
9 the table, although if there was some great objection
10 to that, I mean, we could certainly consider it.

11 What we're really talking about is the
12 variation in dose delivered from that which was
13 prescribed. And so we are considering the Oregon, and
14 secondly, and it's actually does or dosage. So we
15 could conceivably have a medical event involving an
16 intended diagnostic administration, but you would have
17 to exceed the threshold for dose.

18 And actually, I'll give you an example of
19 that. It was an event that occurred and was reported
20 just a few days ago where there was an intent to give
21 four millicuries of Cardiolyte, and the technologist
22 mistakenly administered 400 millicuries of
23 pertechnetate. He simply grabbed the wrong vial out
24 of the ammo box.

25 And you know, the resultant dose to the GI

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1 tract was significant. It certainly exceeded the 50
2 rem. So there's a diagnostic administration, if you
3 will, that is a reportable medical event. So those
4 can occur and obviously do quite frequently.

5 CHAIRMAN MALMUD: Dr. Nag.

6 MEMBER NAG: You read that 20 percent
7 income or intervene that 20 percent income, the fact
8 that 20 percent is the amount that we took for
9 external beam. Now, in terms of external beam, the
10 volumes that are external beam is huge. Whole organs
11 are in it, and therefore, 20 percent over or under
12 does make a significant difference in terms of based
13 in half.

14 But since there was no other criterion, I
15 think it was said, well, that's what we do for
16 external beam. Why not just take that amount for
17 brachytherapy, and that's where that 20 percent came
18 from, not specifically from any act or harm basically
19 given from the 20 percent excess or decrease.

20 Now, when we used the 20 percent as a QA
21 measure to see how we are doing to apply any problem,
22 whether we are going to cause any harm in the patient.
23 I think as QA measure 20 percent is perhaps as good a
24 number as any, and I have no problem if it is used as
25 a QMS.

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1 However, the tendency I have seen, this i
2 may have been true before, may not be true now, I
3 hope, but the tendency I have seen is that this MR is
4 then taken to be the limit at which we'll want to
5 punish somebody. You have given 20 percent more. You
6 have done harm to a patient, and you know, you thereby
7 have to be fined.

8 That I don't agree with. That should be
9 dependent on whether the dose excess is likely to
10 cause any harm in the patient.

11 One of the problems, although we do have
12 a set and stated dose, we really don't even know what
13 dose is required. Many different practitioners would
14 want to give different doses for the same kind of
15 patient.

16 In external beam, that variation is not so
17 much because if you go beyond a certain amount, you
18 cause a big harm in the facing. In brachytherapy,
19 because the organ is so small, you can easily go much
20 higher than 20 percent and not cause harm in the
21 patient.

22 At the same time, because we can give high
23 doses, we prescribe the high doses, and even if we
24 give 20 percent less, we very often will err on the
25 tumor, and this has been born out in human prostate

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1 and many other implants.

2 So, therefore, you want to use the 20
3 percent at the place where you have to allow me
4 (unintelligible), allow the patient, allow MED, no, I
5 don't think so. I think that when you present NTUs
6 you identify any problems. If you want to know
7 whether you are going to help the patient, then you
8 have to do it on a list base basis, not in terms of
9 the dose you gave to the tumor, but in terms of dose
10 you gave to the critical normal tissue.

11 Unfortunately many times we don't even
12 measure the dose in the normal tissue, and that's
13 where we don't know whether we have gone above or
14 below that dose.

15 The other point you have to realize is
16 that dose and implant is dependent on the volume. In
17 a same implant and say I have 100 centigrades or 100
18 brady, you know, set in volume. If we just go half a
19 percent beyond that, you have even 50 percent degree
20 or 50 degree for that same implant.

21 So you know, you can easily now have even
22 on the half by those -- you just increase the volume.
23 On the other hand, say I have even 50 percent more
24 dose if the volume was smaller.

25 Now, that's why I say that this should not

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1 be used to penalize a person.

2 DR. ZELAC: Can I comment?

3 MS. GERSEY: Oh, I was going to comment
4 about enforcement. Were you going to say the same?

5 DR. ZELAC: No, go right ahead.

6 MS. GERSEY: I just wanted to mention the
7 fact that if a medical event does occur, it does not
8 necessarily mean that the NRC takes enforcement action
9 against that licensee. If a medical event occurs and
10 it meets the threshold of reporting, we want to know
11 that to insure that there's not a programmatic problem
12 with that licensee, and that's initially why we set
13 those limits. We want to take a look and make sure
14 there's no underlying issues.

15 Enforcement only occurs if two things
16 happen: there is a violation of the regulations or
17 there's a violation of some other license conditions
18 and their license. So just because a medical event
19 occurs does not mean that automatically they will be
20 penalized and have enforcement action taken against
21 that licensee.

22 DR. ZELAC: Would you also say that most
23 of the time it doesn't result in a penalty?

24 MS. GERSEY: That is correct. Most
25 medical events do not result in enforcement actions.

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1 DR. ZELAC: The second thing I'd like to
2 say with respect to your comments, Dr. Nag, it will
3 depend on what the practitioner had defined as the
4 target volume, which doesn't necessarily have to be
5 the totality of the organ in the prostate, for
6 example, where you might decide that you wish to dose
7 a particular portion of the prostate to a particular
8 dose. The rest of it, you know, what follows
9 accordingly.

10 So really talking about what the
11 practitioner intended versus what the practitioner
12 delivered, and to complete the argument or the
13 statement, we at the last meeting of this advisory
14 committee had four prostate permanent implants
15 specifically tried to develop a criterion that would
16 be suitable for an overdose situation, if you will,
17 and the question that had been raised was whether or
18 not total dose as delivered could be related to total
19 activity implanted.

20 And the answer from OGC, our Office of
21 General Counsel, is that, yes, the two can be
22 considered equivalent. So on that basis if the
23 practitioner had intended, for example, to deliver 100
24 millicuries of iodine in seed form to a particular
25 portion of the prostate and, in fact, delivered less

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1 than 80 to that same portion of the prostate, that
2 would be considered a medical event.

3 Similarly, if the same practitioner had,
4 in fact, implanted 120 millicuries when originally 100
5 had been intended, unlikely to occur, but you know,
6 maybe the wrong seed strength was actually
7 administered as compared to what was intended. That
8 also would be a medical event, not a violation
9 necessarily, but a reportable medical event.

10 CHAIRMAN MALMUD: Thank you.

11 Does that mean that what we are hearing
12 from one another is that we believe that the 20
13 percent figure should be sustained; that we agree that
14 penalties -- that it's a good means of monitoring
15 accuracy; and that we also agree with staff that
16 penalties are not automatically imposed when the 20
17 percent figure is exceeded in one way or another?

18 Dr. Williamson?

19 MEMBER WILLIAMSON: Well, do you want me
20 to answer your question or --

21 CHAIRMAN MALMUD: Yes.

22 MEMBER WILLIAMSON: -- make the comment I
23 was going to make?

24 CHAIRMAN MALMUD: Yes, because it's three
25 minutes before five, and it would be wonderful if we

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1 could end the meeting on time.

2 (Laughter.)

3 MEMBER WILLIAMSON: Well, I think that
4 certainly from my perspective I would say yes in
5 general, but there are some qualifications to be made.
6 I think that traditional brachytherapy was not image
7 guided brachytherapy, and fairly traditional dose
8 specification endpoints were used, such as minimal
9 dose, minimum dose to the periphery of the implanted
10 volume, milligram hours from various other fairly
11 simple, straightforward quantities to calculate.

12 I think one thing is imaging is used more
13 and more, and as you get a more precise measure of
14 exactly where the sources are in relation to the
15 organs, you know, you will find there are significant
16 variations from the pre-plant. This is inevitable.
17 It is a consequence of our inability to position the
18 radioactive sources, you know, as accurately as we can
19 measure where they are with imaging modality.

20 So that means it is almost inevitable that
21 in any implant there will be at least one voxel of
22 tissue where the dose exceeds the planned dose by 20
23 percent or 50 percent or any criterion you'd want to
24 have.

25 So I think the challenge, even if you sort

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1 of accept that QA or sort of technical performance in
2 implementing the physician's prescription, that's the
3 main endpoint here. Even if you accept that, the
4 trick or the challenge technically is to come up with
5 a criterion that doesn't create a huge, unnecessary
6 bushel of medical events that represent the normal
7 variations of acceptable practice.

8 So you know, it's always possible to take
9 this criterion or any other and apply it in some sort
10 of focused, clinically irrelevant way where you
11 generate a huge number of medical events. If you
12 applied minimum dose to the prostate as the criterion,
13 you would find even in the hands of very good
14 practitioners there are enormous fluctuations in the
15 minimum dose given to the prostate even though the
16 preplanning is based upon giving a minimum dose of 145
17 grade, for example.

18 So we've moved away from that criterion in
19 the field as a consequence.

20 CHAIRMAN MALMUD: Dr. Nag.

21 MEMBER NAG: I think that my comment is
22 somewhat similar to Jeff's in that it would depend on
23 how you define your target. You are saying you are
24 going to prescribe a certain dose to your target, and
25 if the dose varied by more or less than 20 percent,

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1 then it's a medical event where except for your
2 target.

3 Now, you say, well, I want to implant the
4 prostate. Where exactly the prostate? Are you going
5 to take the prostate with the one millimeter margin,
6 two millimeter margin?

7 In brachytherapy, even one or two
8 millimeters make a lot of this difference, and
9 therefore, you know, using the 20 percent as a medical
10 event as something to be worried about, it's not
11 really usually a problem because in the prostate I can
12 tell you we are trying to shoot for 145 Grays for an
13 iodine implant. You can control the tumor with 110
14 Gray or 100 Gray, and that is more than 20 percent.

15 Even if you put the exact number of
16 material you wanted, the dose may vary because of the
17 exact position of the seeds. It could even go higher,
18 and therefore, that rad is 20 percent and it tends to
19 worry me if you're going to use it as something other
20 than just to identify in the permanent implant.

21 In the renewable implant, we can control
22 the dose a little better because you are putting the
23 catheters in. You are then calculating, and you are
24 then removing when you have delivered your dose. So
25 in the removable implant, 20 percent is a much better

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1 standard to follow.

2 But in the permanent implant I don't think
3 so.

4 CHAIRMAN MALMUD: Having heard these
5 comments with illustrative examples, is the
6 recommendation that we stay with the 20 percent?

7 MEMBER NAG: It depends what you are using
8 it for. It all depends what you are using that 20
9 percent for.

10 For example, you know, you have a
11 department where you have a QA. Are you using it say,
12 "Well, are we doing anything wrong?" or are you going
13 to use it then strike and have the whole NRC doing a
14 major investigation of your department?

15 You know, some of the people may be
16 overzealous and say, "Well, you exceeded the 20
17 percent to take what it says, and therefore, you are
18 now going to depend on" -- it all depends on what you
19 are using it for.

20 CHAIRMAN MALMUD: Has the NRC behaved in
21 an overzealous fashion where the number of 20 percent
22 has been exceeded?

23 MEMBER NAG: In many cases that, you know,
24 I do not need to go into, but in many institutions
25 yes.

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1 (Laughter.)

2 CHAIRMAN MALMUD: In that case would you
3 recommend a number of 25 or 30 percent? In other
4 words, what I'm trying to drive to is that we
5 recognize that if we have variable numbers for
6 different situations, we will create a level of
7 confusion that doesn't exist currently. So are we
8 pleased with the 20 percent but we would like to put
9 a corollary on it, meaning that administrative action
10 need not be implemented if the 20 percent is exceeded,
11 but that the 20 percent figure should serve as an
12 alert to whoever is running or has responsibility for
13 the individual department, that its own figure should
14 be monitored internally.

15 Dr. Williamson.

16 MEMBER WILLIAMSON: I think this is the
17 wrong question.

18 CHAIRMAN MALMUD: What do you think is the
19 right question?

20 MEMBER WILLIAMSON: Okay. The right
21 question is 20 percent of what?

22 DR. ZELAC: That's very straightforward.
23 It's 20 percent of the prescribed dose. Now, if you
24 wanted to, for example, in Dr. Nag's case, say that
25 you were willing to accept a range of doses to be

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1 delivered to the target organ and if you were outside
2 of that range, you wanted to say that's considered a
3 medical event, don't forget when I started out we said
4 that we were going to look at plus or minus 20 percent
5 as applicable to all modalities collectively or look
6 at individual modalities.

7 If there are exceptions to the plus or
8 minus 20 percent --

9 MEMBER WILLIAMSON: I think the answer
10 you've given is too --

11 CHAIRMAN MALMUD: Wait. He's been waiting
12 very patiently.

13 MEMBER SULEIMAN: What I think I would
14 assume as the event reports come in, you would notice
15 that a new examination is getting a higher report
16 rate. So at that point you'd say, wait a minute.
17 There's something here you'd pay more attention.

18 But we'd have to trust you to do that in
19 terms of policy. If there's a very, very well
20 established procedure where nobody is reporting and
21 all of a sudden you've got something at 20 percent,
22 obviously you know, it's an issue, but if it's
23 something that is infrequently conducted and they come
24 in with a 30 percent report, I think for the first
25 time for that examination I would assume you'd be a

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1 little bit more lenient. You'd look at it a little
2 bit more closely.

3 DR. ZELAC: Well, that is exactly the
4 point. This is to become aware of what is going on.
5 It's not to say that there is going to be remedial
6 measures required. It doesn't mean to say there'
7 going to be any action taken on any regulator's part
8 with respect to the particular licensee, but it's for
9 knowledge to see where we are and where we're going.
10 That's what this is all about.

11 The Commission would like to know what's
12 going on.

13 CHAIRMAN MALMUD: Dr. Nag was next.

14 MEMBER NAG: Yes. This is a new mindset
15 you have given to us. I mean radiation oncologists
16 normally prescribe a certain dose. We have not yet
17 been in the habit of prescribing a range of doses.

18 If you have that as a range of dose, I
19 think that does solve a problem in that the
20 technician would know what range of doses are
21 acceptable for a certain organ. Like in the prostate
22 instead of prescribing 125 Gray, I would now prescribe
23 something -- at the beginning state we are accepting
24 between 100 to 200 Gray, and when it could go 20
25 percent below or above that, that would be a problem.

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1 In the removable implant, I would say
2 5,000 Centigrade, and you know, anything below and
3 above 5,000 would be that 20 percent. I think that is
4 a very good idea.

5 DR. ZELAC: Yeah, I'm not sure that this
6 would fly, but it was offered by analogy to what's
7 submitted for dosages, where the practitioner can
8 either state a particular dosage that's going to be
9 administered or a range of dosages which are
10 considered acceptable.

11 If the administered dose is out of the
12 range, it's reportable as a medical event, you know,
13 assuming that the dose criteria are also met. If the
14 administered dosage differs from the prescribed dosage
15 where there's a given number, one number, by plus or
16 minus 20 percent, it, again, is reportable as a
17 medical event.

18 So my suggestion was simply that perhaps
19 for brachytherapy, permanent implants, something more
20 along those lines than a stated dose would be worth
21 considering.

22 CHAIRMAN MALMUD: Dr. Diamond.

23 MEMBER DIAMOND: Ron, if I may, I've spent
24 a lot of time thinking is there a better way that we
25 can do this. That is the question you're asking us

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1 today, and to paraphrase the former Supreme Court
2 Justice, I don't mean to be too glib. When he was
3 asked about defining pornography, "I can't define it,
4 but I know it when I see it."

5 I cannot think of a single better
6 benchmark that can go and account for all of the
7 vagaries of the clinical scenarios and the different
8 techniques. Therefore, I think that it is reasonable
9 to keep as a benchmark what we're using right now with
10 the clear understanding that in many cases this
11 differential requires no enforcement and actually may
12 be beneficial and as a corollary there are instances
13 in which a difference of less than 20 percent is
14 actually much more serious and actually may warrant
15 some type of corrective action.

16 So having come to the conclusion that at
17 this point I can't think of anything that is more
18 useful, more definable, more practicable, perhaps this
19 is a reasonable benchmark with which to stay with the
20 understanding that judgment must be used all around.

21 CHAIRMAN MALMUD: Dr. Eggli.

22 MEMBER EGGLI: And I think the issue here
23 is that the regulated community sees almost a one-to-
24 one relationship between event reporting and
25 enforcement action; that they worry that if they

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1 report an event, there's going to be an enforcement
2 action.

3 Maybe what this needs is a little more
4 definition in terms of the history where you say, in
5 fact, only a small portion of events result in
6 enforcement. Maybe it needs a policy statement that
7 says that once the evaluation threshold has been
8 reached, that adverse consequences will be considered
9 as a major criteria for considering an enforcement
10 action.

11 So that I think that what you're seeing
12 here is the worry of the regulated community that
13 there's a tight coupling between reporting and
14 enforcement, and if it becomes clear to the regulated
15 community that the intent is to collect data and not
16 necessarily rain down on the reported event, and that
17 there is something other than having crossed the
18 threshold associated with enforcement action, that
19 maybe the threshold again becomes a less fearsome
20 thing for the regulated community.

21 DR. ZELAC: So in terms of knowledge to be
22 passed on, in this case we're not talking about
23 knowledge to the general public. We're talking about
24 knowledge to the general community about what the
25 medical event really means to them.

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1 MEMBER EGGLI: Yes, yes.

2 CHAIRMAN MALMUD: Ralph, did you want to
3 say something?

4 MEMBER LIETO: Yes. Actually it's sort of
5 a takeoff on what Dr. Eggli just said in that maybe
6 what needs to be brought back to the NRC from the
7 medical community is for the specific modalities that
8 have been discussed, where are there really potential
9 risks that we need to look at for the patient being
10 harmed and so forth?

11 For example, everybody has been talking
12 about the prostate. A radiation oncologist told me
13 that, you know, "If I give more than 50 percent to the
14 prostate, that doesn't bother me." He said, "Now, if
15 I give less than 50 percent or less than 30 percent,
16 then I'm going to be concerned."

17 But, you know, being more doesn't
18 necessarily mean -- and I think maybe those are the
19 types of things that might need to be brought back to
20 the NRC, where we look at modality specific issues,
21 not what grow into the regulations, but where do we
22 need to really concern ourselves with does a medical
23 consultant need to be brought in, and so forth and so
24 on, for the NRC.

25 And I think that's part of the issue of

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1 where you want to know where there's an action level.
2 So there would be actually sort of a policy tier what,
3 you know, there's risk for medical harm or two,
4 whereas the other one was just a reporting to see if
5 there's maybe some issues with the licensee that need
6 to be further brought up.

7 CHAIRMAN MALMUD: Dr. Zelac, it seems as
8 if the spirit of the committee is that the 20 percent
9 figure should be maintained and used as a guideline by
10 the physicians for monitoring their own behavior and
11 should not be over reacted to by the NRC unless there
12 is a significant breach or pattern which puts patient
13 health at risk.

14 Is that a fair summary of what you've all
15 said?

16 MS. SCHWARZ: Yes.

17 CHAIRMAN MALMUD: Dr. Williamson, do you
18 disagree with that statement?

19 MEMBER WILLIAMSON: A little. I mean, I'm
20 okay with saying 20 percent is fine. I within limits
21 would accept the idea of 20 percent of the prescribed
22 dose, but I think this covers up the fact that there
23 really is a technical problem here to be solved, and
24 that is practitioners use prescribed dose in a way
25 that doesn't have regulatory significance, and you

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1 know, the actual dose delivered in a permanent
2 implant, depending upon how the criterion of
3 prescribed is defined, would easily exceed 20 percent,
4 but if different criteria were picked, it wouldn't.

5 So I think you're stuck with the technical
6 problem of coming up with a meaningful criterion that
7 detects really bad implants, technically avoidable
8 errors which really are of key way significance versus
9 insignificant events from a key way concern
10 perspective.

11 And I don't think that either you or the
12 community wants to report to you a huge number of
13 technically or clinically and technically irrelevant
14 events because whether there's an enforcement action
15 or not, you know, basically licensees, even an
16 unscheduled visit by you is a punishment. They use,
17 you know, an intrusive investigation as a punishment.

18 DR. ZELAC: Let me note that the plus or
19 minus 20 percent is applicable to brachytherapy,
20 including permanent implants has been in place for
21 many years, and we have not been experiencing either
22 the previous version of the rule nor the current
23 version of the rule, which makes it clearer that it's
24 20 percent perhaps for some, a rash of reported
25 medical events.

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1 However, this is the advisory committee.
2 We're looking to you for advice. If we can get some
3 advice from certain select members or the committee as
4 a whole on what might be a better criteria to use for
5 permanent implant brachytherapy, we'd more than
6 welcome it.

7 CHAIRMAN MALMUD: Dr. Schwarz.

8 MEMBER WILLIAMSON: Talking about that is,
9 I guess, my point.

10 CHAIRMAN MALMUD: Dr. Schwarz.

11 MEMBER WILLIAMSON: There's work to be
12 done.

13 MS. SCHWARZ: I think maybe something to
14 consider is that the NRC could come to the committee
15 when there are instances of potentially exceeding 20
16 percent in some of these types of therapeutic
17 modalities and discuss with the medical community what
18 this really means. Is it significant or is it not
19 significant?

20 DR. ZELAC: Well, you may recall that at
21 the last meeting and the previous meeting what we were
22 discussing, in fact, was a place where it was
23 significant in that there were a series of patients
24 that had been under dosed in prostate implants, and as
25 a result, there were recurrences.

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1 So, yes, when there are situations that
2 seem to warrant input and consideration by the
3 committee, we are doing that already and we will
4 continue to do that.

5 MS. SCHWARZ: I just think it's difficult
6 to regulate this situation.

7 DR. ZELAC: Yes.

8 MS. SCHWARZ: I think that diagnostics is
9 one thing, and therapeutics is more complicated.

10 CHAIRMAN MALMUD: Dr. Eggli.

11 MEMBER EGGLI: Just to reiterate the point
12 that Dr. Williamson made, we can't look back at
13 history on the reporting of these previous events
14 because our ability to detect the errors is becoming
15 increasingly sophisticated and has outstripped our
16 ability to correct those errors.

17 MEMBER WILLIAMSON: That's correct.

18 MEMBER EGGLI: And I think that's the key
19 point that Dr. Williamson is making, in that you have
20 the potential to develop increasing numbers of these
21 because our technology for detection has become very
22 sophisticated.

23 DR. ZELAC: So far we haven't seen it.
24 Maybe the practitioners are using discretion as to
25 what they --

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1 MEMBER WILLIAMSON: I suspect so.

2 DR. ZELAC: -- report as medical events,
3 and I would expect so as well, but getting back, Dr.
4 Malmud, perhaps you'd be inclined to appoint a further
5 subcommittee to consider this issue because if there
6 is something out there that we should be looking at,
7 we'd like to hear about it.

8 CHAIRMAN MALMUD: Well, Dr. Zelac, I'm not
9 certain that the committee feels that there is a
10 better technique. We work in a world of precise
11 estimates, and therefore, as we are able to measure
12 the outcomes better than we could in the past because
13 of improved technology, we have not yet found a better
14 way of judging, but as Dr. Diamond paraphrased one of
15 the Supreme Court Justices, we know when something is
16 really wrong when we see it.

17 It is the wish of the members of this
18 committee who are practitioners that the NRC would
19 also recognize that there are serious breaches which
20 require attention, and there are those which exceed
21 limits which do not require attention. And separating
22 the wheat from the chaff is one of the most difficult
23 things to do.

24 Overzealous enforcement results in
25 unintentional concealment. Rational enforcement

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1 results in a collaborative form of behavior. In the
2 vast majority of cases, the enforcement is rational
3 and results in a collaboration between providers and
4 regulators to the public benefit. And I think what
5 you're hearing is the same thing reiterated in many
6 different ways.

7 We don't have a better way. I don't think
8 anyone at this table is willing to propose a better
9 way. We can critique the current way. We can
10 critique it. We cannot provide you a better solution.

11 That's what I'm hearing. To appoint a
12 subcommittee to come up with a miraculous response is
13 going to be an effort which will not be fruitful.

14 Dr. Williamson is raising his hand.
15 Perhaps he wishes to be a subcommittee of one.

16 (Laughter.)

17 MEMBER WILLIAMSON: I wasn't exactly
18 raising my hand for that purpose, but I do have
19 another comment, and that is maybe you should better
20 define for us what the problem is. Are you trying to
21 respond to arbitrary, but perhaps --

22 DR. ZELAC: No, no, no.

23 MEMBER WILLIAMSON: -- but perhaps
24 misplaced concern of the Commissioners? Are you
25 telling us that you feel you don't have an adequate

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1 regulatory handle over --

2 DR. ZELAC: No, no, no.

3 MEMBER WILLIAMSON: What is the problem?

4 DR. ZELAC: Let us back up. You may
5 recall at the last meeting there was discussion
6 between Dr. Nag specifically and the Commissioners
7 concerning permanent implant prostate brachytherapy
8 and, by extension, other permanent implant
9 brachytherapy, and the appropriateness of using the
10 plus or minus 20 percent criteria for judgment whether
11 or not medical events had occurred in that modality.

12 As a result of that discussion, the
13 Commissioners decided that if we are going to look at
14 that particular modality and the applicability of plus
15 or minus 20 percent to it, that we should as well see
16 if there was and remains a rational basis for using
17 plus or minus 20 percent for all of the other
18 modalities as well.

19 So the question was posed in a broad sense
20 because of the Commission's intent that something
21 should not remain on the books that was inappropriate.
22 We've gotten feedback on all of the modalities
23 essentially with plus or minus 20 percent being
24 reasonable with the possible exception of permanent
25 implant brachytherapy where we started.

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1 So if there is a different way to approach
2 that particular modality, that's what I would like
3 input on.

4 CHAIRMAN MALMUD: That's very helpful
5 because there you're asking us to form a subcommittee
6 to look at a specific mode of therapy --

7 DR. ZELAC: Yes, I am.

8 CHAIRMAN MALMUD: -- and to the exclusion
9 of all other --

10 DR. ZELAC: Yes, that's correct.

11 CHAIRMAN MALMUD: -- techniques that are
12 under the 20 percent rule, and I would ask with
13 humility --

14 (Laughter.)

15 CHAIRMAN MALMUD: -- those members of the
16 radiation oncology community at this table if they
17 feel that this is an issue which they as a
18 subcommittee, meaning they and the physicists who are
19 associated with them, would like to look at as it
20 applies solely to --

21 MEMBER DIAMOND: You should be looking to
22 your left.

23 (Laughter.)

24 CHAIRMAN MALMUD: -- solely to the issue
25 of therapy to the prostate, which is the area of

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1 concern.

2 Dr. Nag.

3 MEMBER NAG: I would say it is worthwhile
4 whether to investigate permanent brachytherapy, not
5 just the prostate, but permanent brachytherapy because
6 of this ambiguity, because the 20 percent rule may or
7 may not apply. It's worthwhile proceeding and perhaps
8 not only in a subcommittee within the ACMUI, but also
9 maybe get the input of a few of the leaders in
10 brachytherapy in the community, maybe get them
11 involved also.

12 CHAIRMAN MALMUD: May I suggest that
13 perhaps the problem would be better addressed by first
14 looking at one application and then extending it
15 beyond that?

16 If after the study of one application is
17 completed because there may be subtleties that are in
18 other forms of therapy that are not found in prostate,
19 and prostate appears to be a problem which is of
20 concern and which this committee has looked at with
21 concern, particularly under therapy, and that would be
22 a good target for us to look at, starting with one and
23 then expanding it if necessary into the future.

24 And Dr. Williamson concurs with me.

25 Ralph.

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1 MEMBER WILLIAMSON: I don't think that
2 necessarily it's permanent versus non-permanent. I
3 actually think it's image based versus non-image based
4 where you have a basis and anatomical information for
5 creating, you know, the appearance of large errors or
6 detecting large errors.

7 DR. ZELAC: Would that be unfortunately
8 encouraging the use of an outdated modality? Would
9 people avoid using imaging --

10 MEMBER WILLIAMSON: No.

11 DR. ZELAC: -- because there was more of
12 a risk?

13 MEMBER WILLIAMSON: I don't think so.

14 DR. ZELAC: I don't think so either,
15 but --

16 MEMBER WILLIAMSON: You could. Well, I
17 mean, there are precedents for your attitude
18 discouraging technical innovation. I'll name post
19 dose rate brachytherapy as one of those which we
20 really did successfully scare off everybody in the
21 United States from using it for ten years. So I
22 wouldn't laugh off the risk.

23 CHAIRMAN MALMUD: I would just add a
24 comment. I have known Mr. Zelac for over 30 years,
25 and I've never known him to have an attitude.

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1 (Laughter.)

2 CHAIRMAN MALMUD: So we'll put "your
3 attitude" in quotations.

4 MEMBER LIETO: I would just ask --

5 CHAIRMAN MALMUD: Dr. Williamson agrees.
6 Ralph.

7 MEMBER LIETO: I would just ask NRC staff
8 if they could go back to the old misadministration
9 rule, as we'll call it, because that's where this 20
10 percent value came from. I'm pretty sure somewhere in
11 those statements that that's where the origin of this
12 came from.

13 I think as one of the other members said
14 earlier, I think it was based on external being
15 teletherapy and the supposed difference in that dosage
16 could affect outcomes or something of that nature, if
17 memory serves me right, but that, you know, we're
18 talking 20-plus years ago when this first came out.

19 But I know that's where it was based in,
20 and I think there were some references that were given
21 at that time, and I think it would provide a nice
22 basis for the subcommittee and also the advisory
23 committee, in general, when this comes back to look at
24 the applicability of that 20 percent value.

25 DR. ZELAC: I started looking at the

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1 statements of consideration for all of the Part 30
2 rules going back. I got back to 1991. I simply ran
3 out of time.

4 MEMBER LIETO: We're talking 1980s.

5 DR. ZELAC: I know. I know. It's in the
6 1985 range, something like that. There might be
7 something in there, and I would hope that there would
8 be.

9 DR. ZELAC: Yes.

10 CHAIRMAN MALMUD: Well, Dr. Williamson is
11 willing to serve on a subcommittee to look at the
12 issue of brachytherapy and the prostate and dosimetry.
13 Do we have other volunteers to participate in this
14 process?

15 MEMBER NAG: I guess I'll have to be in
16 there.

17 CHAIRMAN MALMUD: Dr. Nag.

18 MEMBER WILLIAMSON: I guess you will.

19 CHAIRMAN MALMUD: Sure, and Mr. Lieto.
20 Dr. Williamson, will you take the lead in it?

21 MEMBER WILLIAMSON: Sure.

22 CHAIRMAN MALMUD: Thank you very much.

23 MEMBER WILLIAMSON: And, Dr. Diamond, how
24 would you like to?

25 CHAIRMAN MALMUD: Dr. Diamond.

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1 (Laughter.)

2 CHAIRMAN MALMUD: You told me to look to
3 my left. I listened to you.

4 MEMBER DIAMOND: Thank you.

5 CHAIRMAN MALMUD: And you were speaking in
6 terms of direction, not in terms of politics, and I
7 was happy to do so.

8 MEMBER WILLIAMSON: I do think it would be
9 helpful for there to be a staff person on this
10 subcommittee so that we continue to be focused on the
11 regulatory concerns because that's what we're trying
12 to do.

13 CHAIRMAN MALMUD: We're looking for a
14 staff person to assist.

15 MEMBER WILLIAMSON: Maybe Dr. Zelac would
16 like to help.

17 MR. MILLER: I think Dr. Zelac could
18 certainly provide a link to the subcommittee, but I
19 think if he were to serve on the subcommittee, we're
20 violating --

21 CHAIRMAN MALMUD: All right. Who would
22 you recommend from staff?

23 You don't need to respond immediately.

24 MR. MILLER: Yeah, I mean, I think in one
25 perspective, as he's framed the issue, as a result of

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1 the last Commission meeting, the staff was tasked to
2 seek your counsel and report back to the Commission
3 whether or not there's any recommendations with regard
4 to changes.

5 So anything the subcommittee would do
6 would have to come back to the full committee and then
7 get a formal recommendation back to the staff and
8 we'll go forward.

9 I guess what I would be searching for is
10 what is the need on the part of the subcommittee for
11 a staff --

12 CHAIRMAN MALMUD: I'll let Dr. Williamson
13 define that since it's his request.

14 MR. MILLER: -- interaction, yeah.

15 MEMBER WILLIAMSON: Because we are
16 attempting to define a quality indicator that would be
17 the basis for regulatory action, and so I think it's
18 very important to be able to have the interchange, the
19 access to the data, you know, an opportunity to bounce
20 ideas off.

21 I'm not suggesting the person would be
22 involved in the consensus making, but I do think that
23 as an ex officio member, to keep the Commission
24 perspective close at hand and to be able to provide us
25 data would be very helpful.

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1 MR. MILLER: Well, I would couch that as
2 being you're asking for a staff member to be a link to
3 the subcommittee --

4 MEMBER WILLIAMSON: A liaison.

5 MR. MILLER: -- to provide you the
6 information that you need in order to deliberate on
7 the issue.

8 MEMBER WILLIAMSON: That's right.

9 MR. MILLER: As opposed to be a member of
10 the subcommittee, and with that distinction --

11 MEMBER WILLIAMSON: I think a liaison.

12 MR. MILLER: A liaison. I certainly can
13 support that.

14 MEMBER WILLIAMSON: Or an ex officio
15 member, whatever you want to call it.

16 MR. MILLER: We can certainly support
17 that. I even have someone in mind who is very near me
18 right now.

19 (Laughter.)

20 CHAIRMAN MALMUD: Now, the hour being
21 5:30, one half hour longer than we had anticipated,
22 and our goal for tomorrow being to end on time so
23 those of you who have travel plans which crisscross
24 the country to get back home, wherever you're going to
25 go from here, we will try and adhere to the schedule

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1 tomorrow.

2 I'd like to thank you all and look for a
3 motion for adjournment for today's session.

4 MR. ESSIG: One final comment.

5 CHAIRMAN MALMUD: One comment, Mr. ESSIG.

6 MR. ESSIG: Just real briefly. Just as a
7 heads up for tomorrow morning, the opening 15 minutes
8 will be Dr. Roger Broseus giving you an overview of
9 the proposed final T&E rule, a draft final T&E rule.
10 That, we're going to take 15 minutes.

11 And then we have allocated an hour and 45
12 minutes in the schedule for the committee to formulate
13 any comments on what they've heard and to put that
14 together in some sort of what we'd like ideally is if
15 you could put pen to paper or fingers to keyboard and
16 actually craft at least in rough draft form something
17 that all of you would be agreeable to in terms of
18 recommendation that would come to us, that we could
19 include in the package that goes forward.

20 So just as a heads up, that's --

21 CHAIRMAN MALMUD: We look forward to a
22 stimulating morning meeting.

23 MR. ESSIG: Okay.

24 CHAIRMAN MALMUD: Is there agreement for
25 adjourning?

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1 Oh, Sally, a motion to adjourn.

2 Seconded?

3 PARTICIPANTS: Second.

4 CHAIRMAN MALMUD: All in favor.

5 (Chorus of ayes.)

6 CHAIRMAN MALMUD: Thank you all.

7 (Whereupon, at 5:29 p.m., the meeting in
8 the above-entitled matter was adjourned.)

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