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1 UNITED STATES OF AMERICA

2 NUCLEAR REGULATORY COMMISSION

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4 ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

5 + + + + +

6 TELECONFERENCE

7 + + + + +

8 THURSDAY,

9 DECEMBER 18, 2008

10 + + + + +

11 The meeting was convened telephonically at
12 1:00 p.m., Leon Malmud, ACMUI Chairman, presiding.

13 MEMBERS PRESENT:

14 LEON MALMUD, Chairman

15 RICHARD VETTER, Vice Chairman

16 DOUGLAS EGGLI, Member

17 DARRELL FISHER, Member

18 DEBBIE GILLEY, Member

19 RALPH LIETO, Member

20 STEVE MATTMULLER, Member

21 SUBIR NAG, Member

22 ORHAN SULEIMAN, Member

23 BRUCE THOMADSEN, Member

24 WILLIAM VANDECKER, Member

25

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1 PRESENT (cont.)

2 MICKEY GUIBERTEAU, Diagnostic Radiologist

3

4 NRC HQ STAFF PRESENT:

5 CHRIS EINBERG, DFO

6 JAMES FIRTH

7 CYNTHIA M. FLANNERY, ALT DFO

8 DONNA-BETH HOWE

9 SOPHIE LE

10 ROB LEWIS

11 GRETCHEN RIVERA-CAPELLA

12 ASHLEY TULL

13 GLENDA VILLAMAR

14 DUANE WHITE

15 RONALD ZELAC

16

17 NRC REGIONAL STAFF PRESENT:

18 COLLEEN CASEY

19 JACKIE COOK

20 SANDY GABRIEL

21 PATTY PELKE

22 TOM THOMPSON

23

24

25

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1 OTHERS PRESENT:
2 CHERYL BEEGLE, NIH
3 LUCA BRIGATTI
4 CLARA C. CHEN, NIH
5 WILLIAM DAVIDSON, University of Pennsylvania
6 JEFF HEIER, NeoVista
7 JOHN HENDRICK, NeoVista
8 PETER HERSCOVITCH, NIH
9 KAREN LANGLEY, University of Utah
10 MIKE PETERS, American College of Radiology
11 BARRY SIEGEL
12 MIKE STABIN, Vanderbilt University
13 CINDY TOMLINSON, Society of Nuclear Medicine
14 BILL VERMEERE, NeoVista

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

(1:02 p.m.)

1
2
3 MR. EINBERG: I'm going to open up the
4 meeting. As the Designated Federal Officer for this
5 meeting, I would like to welcome you to this
6 teleconference public meeting of the Advisory
7 Committee on the Medical Uses of Isotopes.

8 I am the Chief of the Medical Safety and
9 Events Assessment Branch. I have been designated as
10 the federal officer for this Advisory Committee in
11 accordance with 10 CFR Part 7.11.

12 Present today as the alternate designated
13 federal officer is Cindy Flannery, team leader for the
14 Medical Radiation Safety Team.

15 This is an announced meeting of the
16 Committee being held in accordance with the rules and
17 regulations of the Advisory Committee Act and the
18 Nuclear Regulatory Commission. This meeting was
19 announced in the September 22, 2008, edition of the
20 Federal Register, Volume 73, page 54635.

21 The function of the committee is to advise
22 the staff on issues and questions that arise on the
23 medical use of isotope material. The committee
24 provides counsel to the staff but does not determine
25 or direct the actual decisions of the staff or the

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1 Commission. The NRC solicits the views of the
2 committee and values their opinions.

3 I request that, whenever possible, we try
4 to reach consensus on the procedural issues that we
5 will discuss today. We also recognize there may be a
6 minority or a dissenting opinion. If you have such
7 opinions, please allow them to be read into the
8 record. At this point, I would like to perform a roll
9 call of the ACMUI members that may be participating
10 today.

11 Dr. Leon Malmud, Chairman, Health --

12 CHAIRMAN MALMUD: Here.

13 MR. EINBERG: -- Care Administrator?

14 CHAIRMAN MALMUD: Here.

15 MR. EINBERG: Dr. Richard Vetter, Vice
16 Chairman, Radiation Safety Officer?

17 VICE CHAIRMAN VETTER: Here.

18 MR. EINBERG: Dr. Douglas Eggli, Nuclear
19 Medicine Physician?

20 MEMBER EGGLI: Here.

21 MR. EINBERG: Dr. Darrell Fisher, Patient
22 Advocate?

23 MEMBER FISHER: Present.

24 MR. EINBERG: Ms. Debbie Gilley, State
25 Government Representative?

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1 (No response.)

2 I just understand Debbie will be joining
3 us late.

4 Mr. Ralph Lieto, Nuclear Medicine
5 Physicist?

6 MEMBER LIETO: Present.

7 MR. EINBERG: Mr. Steve Mattmuller,
8 Nuclear Pharmacist? Is Mr. Mattmuller there?

9 MEMBER MATTMULLER: Yes, I'm here. Sorry.

10 MR. EINBERG: Okay. Thank you. And Dr.
11 Subir Nag, Radiation Oncologist? Dr. Nag?

12 (No response.)

13 Dr. Orhan Suleiman, FDA Representative?

14 MEMBER SULEIMAN: Yes, here.

15 MR. EINBERG: Dr. Bruce Thomadsen, Medical
16 Physicist Therapy?

17 (No response.)

18 Dr. William VanDecker, Nuclear
19 Cardiologist?

20 MEMBER VANDECKER: Here.

21 MR. EINBERG: Dr. James Welsh, Radiation
22 Oncologist?

23 (No response.)

24 Okay. I believe we have a quorum. Dr.
25 Mickey Guiberteau is representing the Diagnostic

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1 Radiologists. Dr. Guiberteau does not --

2 THE COURT REPORTER: This is the Court
3 Reporter. I'm having a difficult time hearing you due
4 to the static.

5 (Whereupon, at 1:06 p.m., the proceedings in the
6 foregoing matter went off the record
7 briefly, during which time the static
8 problem was corrected.)

9 MR. EINBERG: Okay. Let me just -- the
10 Court Reporter indicated that he was having some
11 trouble hearing me. I'll repeat some of it.

12 Dr. Mickey Guiberteau is representing the
13 Diagnostic Radiologists. Dr. Guiberteau does not have
14 voting privileges, but he will speak on behalf of the
15 Diagnostic Radiologists. I would like to thank Dr.
16 Guiberteau for acting in this capacity.

17 I now ask NRC staff members who are
18 present to identify themselves. I'll start with the
19 individuals in the room here, and then we'll turn it
20 over to the other NRC staff members on the phone.

21 MR. LEWIS: This is Robert Lewis from
22 FSME.

23 MS. FLANNERY: Cindy Flannery, FSME.

24 MR. FIRTH: James Firth, FSME.

25 DR. ZELAC: Ron Zelac, FSME.

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1 MR. WHITE: Duane White, FSME.

2 MS. RIVERA: Gretchen Rivera, FSME.

3 MS. VILLAMAR: Glenda Villamar, FSME.

4 MS. LE: Sophie Le, FSME.

5 MS. TULL: Ashley Tull, FSME.

6 MR. EINBERG: Okay. Now, for regions,
7 anyone from Region I?

8 MR. THOMPSON: Tom Thompson in the
9 Commercial Branch.

10 MS. GABRIEL: And Sandy Gabriel.

11 MR. EINBERG: Okay. Thank you.
12 Region III?

13 MS. PELKE: Patty Pelke from the Materials
14 Licensing Branch.

15 MR. EINBERG: Thank you. Region IV?
16 Okay.

17 DR. HOWE: And Donna-Beth Howe from
18 Headquarters.

19 MR. EINBERG: Okay. Thank you, Donna-
20 Beth. Is that it for the NRC staff?

21 MS. COOK: Jackie Cook, Region IV.

22 MR. EINBERG: Okay. Thank you.

23 Next, I would ask members of the public
24 who are participating on the phone if they would
25 identify themselves, please. For the Court Reporter,

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1 if you could please spell out your name.

2 PARTICIPANT: My name is -- oh, you're
3 going to spell the name for the public?

4 MR. EINBERG: Okay. Yes. Ashley Tull
5 here is saying that you don't need to spell out your
6 name.

7 MS. TULL: If you have notified me via
8 e-mail previously, I have your name on the list
9 already spelled for the Court Reporter.

10 MR. SIEGEL: Okay. This is Dr. Barry
11 Siegel. I'm here.

12 MR. VERMEERE: Bill Vermeere from
13 NeoVista.

14 DR. BRIGATTI: This is Dr. Luca Brigatti.
15 I'm an ophthalmologist.

16 MR. HENDRICK: John Hendrick from
17 NeoVista.

18 MS. TOMLINSON: This is Cindy Tomlinson
19 from the Society of Nuclear Medicine.

20 DR. HERSCOVITCH: This is Dr. Peter
21 Herscovitch from the NIH, Bethesda, Maryland. And in
22 the room we also have Dr. Clara Chen from Nuclear
23 Medicine at the NIH, and Cheryl Beegle from the NIH.

24 MR. DAVIDSON: This is Will Davidson from
25 the University of Pennsylvania.

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1 MS. LANGLEY: Karen Langley, University of
2 Utah, Salt Lake City.

3 MR. PETERS: This is Mike Peters, American
4 College of Radiology.

5 MR. STABIN: Mike Stabin, Vanderbilt
6 University.

7 MR. EINBERG: Okay. Is there anybody else
8 on the line who has not announced their participation?

9 MS. CASEY: This is Colleen Casey, NRC,
10 Region III.

11 MR. EINBERG: Okay. Very good. We'll
12 move on.

13 Dr. Leon Malmud, ACMUI Chairperson, will
14 conduct today's meeting. Following the discussion of
15 each agenda item, the chair, at his option, may
16 entertain comments or questions from members of the
17 public who are participating with us today.

18 At this point, I would like to turn the
19 meeting over to Rob Lewis, who would like to make a
20 few opening comments. And then, we will turn the
21 meeting over to Dr. Malmud.

22 And just one last reminder, for those
23 people who joined us late, please press star 6 to mute
24 your phone if you are not speaking.

25 Thank you.

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1 Rob?

2 MR. LEWIS: Thank you. Good afternoon,
3 everyone. I would like to just bring the committee up
4 to speed on a couple of activities occurring within
5 NRC that are getting a lot of attention, the first of
6 which is the national source tracking system. We do
7 have a regulation which requires all licensees to
8 enter the sources and the transactions of sources for
9 IAEA Category 1 and 2 sources -- so, basically, the
10 increased controls licensees -- into the national
11 source tracking system by January 31st of 2009.

12 The system has received its authority to
13 operate, which is a step under federal information
14 security requirements, and is available at this point.

15 In order to use the system, you have to go through an
16 extensive credentialing program and receive tokens
17 that you plug into your computer to make sure that the
18 users have proper credentials and are actually the
19 users. There is a very high level of security for a
20 federal information system.

21 And, in all honesty, the credentialing
22 process is not going very smoothly at this point. So
23 for those of you that are in the meeting that are
24 licensees, I would encourage you to get involved with
25 that early. There is currently NSTS training going on

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1 around the country, and the credentialing process
2 itself is rather onerous. But it is nothing that we
3 can control from the program office perspective. So
4 it is difficult, and we are working through issues.

5 We underestimated the precision with which
6 applicants need to enter information. For example, if
7 you enter your licensee name and it doesn't match a
8 database of companies that the credentialing
9 contractor uses, then you will get rejected from the
10 system. If you enter "corporation" instead of "inc,"
11 if your official company name is Something Something,
12 Inc., you would be rejected.

13 So things like that that we need to work
14 through, and we are working through, but the
15 regulation is set. And the compliance with the rule
16 is mandated as January 31st people -- licensees need
17 to be entering their source information.

18 Now, using the NSTS website is only one
19 option for compliance with that rule. There are other
20 options of providing the information by fax or e-mail
21 to NRC or an agreement state. So those options exist,
22 but we want to create a situation where people want to
23 use the NSTS because it is efficient once you get into
24 it. Getting into it is the trick.

25 The second topic area is safety culture.

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1 The NRC has several activities underway regarding
2 safety culture, both internal safety culture for the
3 agency and external safety culture for licensees. I
4 would like to touch a little bit on the second piece
5 of that, the external safety culture.

6 Our safety culture is basically a
7 corporate attitude from the worker all the way through
8 senior management that is a personal dedication and
9 accountability towards safety issues. And it is often
10 synonymous, for example, with Safety First attitude,
11 willing to stop work if they think something is unsafe
12 and the management would support them, willingness to
13 stop it.

14 It is a concept that has been around for
15 reactors for maybe 10 years now, but it really caught
16 a lot of focus after the Davis-Besse vessel head
17 erosion that occurred about five years ago. And the
18 Commission has directed the NRC staff to look at
19 extending safety culture into the materials area and
20 extending safety culture concepts into the source
21 material security issue, or just security area in
22 general, or a security culture if you will.

23 The staff are working on those assignments
24 from the Commission, and in the near future we will be
25 engaging the committee more on our efforts to get user

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1 feedback on how safety culture could be applied to
2 materials, including medical applications.

3 There is a public workshop currently
4 planned for January 28th at NRC Headquarters on this
5 area. The main focus is soliciting input from the
6 stakeholders and the public. The workshop will just
7 be one opportunity for NRC to obtain the views of the
8 stakeholders.

9 We will be engaging the committee in the
10 next several months, next few months I should say. We
11 owe something to the Commission in about four months,
12 not the final answer but our initial proposals to the
13 Commission. So more to come on that topic, but it is
14 an emergent issue that will need some attention in the
15 near future.

16 And, finally, I want to thank the
17 committee members for completing the information
18 security training. We do have several periodic
19 trainings throughout the year, various -- invariably,
20 they have bad timing of when they are announced, and
21 this one happens to be due over Christmas and New Year
22 break. But I appreciate what you did to get -- make
23 sure that you did your part as committee members.

24 That is a requirement placed upon NRC, as
25 is many of the other periodic training requirements.

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1 I realize that you have to take time out of your busy
2 schedules to do those. But the management of NRC is
3 held very accountable to making sure everyone has
4 jumped through all the hoops on all of those periodic
5 training requirements.

6 At this point, if Dr. Malmud will indulge
7 me, I would be willing to take any questions from the
8 committee members before we get started on general
9 topics.

10 CHAIRMAN MALMUD: Are there any questions?

11 This is Malmud. Are there any questions?

12 (No response.)

13 MR. LEWIS: Thank you, Dr. Malmud. I will
14 turn the meeting over to you.

15 CHAIRMAN MALMUD: Thank you. We have the
16 next item on the agenda, which will be Cindy Flannery.

17 Am I correct, Cindy?

18 MS. FLANNERY: Yes. Cindy Flannery. The
19 topic of this first discussion is NRC's position on
20 the applicability of the medical event reporting
21 criteria for an event that was reported to the NRC
22 involving an infiltration of F-18 of FDG.

23 NRC staff's objective here today is to get
24 ACMUI's input on whether NRC staff should pursue a
25 change to our current position on the lack of

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1 reportability of infiltrations of dosages that may
2 result in doses that exceed the dose threshold in the
3 medical event reporting criteria -- that is, 50 rem to
4 an organ or tissue.

5 An event was reported earlier this year as
6 possible medical event. 3.6 millicuries of F-18 FDG
7 was infiltrated into the anacubital dermis adjacent to
8 the left elbow. The dose of the tissue was estimated
9 to range somewhere between 200 millirem and 96 rem,
10 and it was based on assumptions such as the entire
11 dose was infiltrated into a tissue of 60 cubic
12 centimeter volume sphere using a soft tissue density
13 of 1.06 gram per cubic centimeter with a range of mean
14 resonance time of .006 to 2.6 hours.

15 So just a little bit more background on
16 this, the needle was carefully checked for
17 infiltration using a 10 milliliter flush and a 100
18 milliliter infusion prior to injection of the F-18
19 FDG. The infiltration was discovered upon image
20 acquisition one hour after the administration, and,
21 unfortunately, the biological parameters were not
22 measured, so it lead to a very large and varied
23 absorbed dose estimates, as listed in slide 3.

24 But there were no identified adverse
25 effects. There was nothing to suggest any kind of a

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1 radiation injury.

2 The licensee did file a report 30 days
3 after the event, and they stated that, "Because the
4 technologist noted the diffuse localization of the F-
5 18 FDG, it seems likely that much of the administered
6 dose did not -- or, I'm sorry -- did get into the
7 vein, leaving less than 3.6 millicuries to irradiate
8 the local area."

9 NRC's internal dose assessor did review
10 the licensee's dose estimates, as provided on slide 3,
11 and found this to be reasonable. Using a different
12 method, NRC's calculations were slightly lower, but,
13 as I said, they were certainly reasonable.

14 Now, as far as the outcome, the event was
15 later retracted because NRC staff determined that an
16 infiltration does not require reporting as a medical
17 event. Based on some supplementary information that
18 supported the previous equivalent regulation -- 35.33
19 -- which states -- and it's in 45 Federal Register
20 31703, May 14, 1980, "Extravasation is the
21 infiltration of injected fluid into the tissue
22 surrounding a vein or an artery. Extravasation
23 frequently occurs in otherwise normal IV or intra-
24 arterial injections. It is virtually impossible to
25 avoid. Therefore, the Commission does not consider

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1 extravasation to be a misadministration."

2 So based on these excerpts from the
3 statement of consideration that I just quoted, it was
4 staff's determination at that time that this case did
5 not qualify as a medical event. It has always been
6 NRC's position that infiltrations do not constitute a
7 medical event.

8 But that position has been based on the
9 fact that diagnostic dosages, like technetium-99m,
10 that were typically used in nuclear medicine at the
11 time are gamma emitters of relatively low energy and
12 low risk and wouldn't exceed the dose thresholds that
13 are in the medical event criteria.

14 The language in the FRN is not really
15 based on a distinction between diagnostic and
16 therapeutic administrations, but, rather, on the fact
17 that some of that, such as infiltrations, are an
18 integral part of the procedure, and so their
19 occurrence must be viewed as expected.

20 At the time that this FRN was published,
21 higher energy radiopharmaceuticals, like PET
22 radiopharmaceuticals, were just not being used. This
23 is from 1980, as I mentioned before.

24 F-18 is a diagnostic administration, but
25 because of the higher energies that can now result in

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1 a dose to the surrounding tissue exceeding 50 rem,
2 when doses are infiltrated, NRC is trying to determine
3 whether there is any justification based on safety
4 significance to change NRC's policy for these new NARM
5 materials, which are now under our regulatory
6 authority, and also the applicability of the medical
7 event criteria for infiltrated dosages.

8 And just to take it one step further,
9 should there be a requirement for reporting an
10 infiltration of a therapeutic administration, that is
11 something that also has not been considered before.

12 So that concludes my opening of the
13 discussion.

14 CHAIRMAN MALMUD: Thank you, Cindy.

15 Any comments or discussion regarding the
16 issue of infiltration of F-18 FDG? I heard someone
17 click on or click off.

18 MEMBER THOMADSEN: That is Bruce joining
19 you. Sorry I am late. I had a patient who was
20 considerably late today.

21 CHAIRMAN MALMUD: Thank you for joining
22 us. Cindy just presented the material regarding the
23 infiltration of F-18 FDG and therapeutic
24 radiopharmaceuticals. I was asking the group if there
25 are any comments regarding her presentation.

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1 VICE CHAIRMAN VETTER: Dr. Malmud, this is
2 Dick Vetter.

3 CHAIRMAN MALMUD: Dr. Vetter?

4 VICE CHAIRMAN VETTER: I just wanted to
5 point out that there is -- it's a bit old, but there
6 is a publication that looked at infiltrations of
7 radiopharmaceuticals back in 1994, Castronovo, et al.,
8 and the -- they looked at infiltration of various
9 volumes, various volumes of tissue, etcetera.

10 And just as an example, maximum specific
11 activity for a thallium -- let's see, infiltrations of
12 thallium at the maximum specific activity available in
13 two gram volume of tissue, worst case possible, would
14 produce skin radiation burden of 417 to 463 rads. If
15 you look at the table in that particular publication,
16 which I can share with the staff if they don't have
17 it, the doses range from about 40 rads to over 500,
18 almost 600.

19 So the doses from infiltration are
20 potentially significant. In fact, they are quite a
21 bit higher than that particular PET issue that she
22 outlined.

23 CHAIRMAN MALMUD: Thank you.

24 MEMBER NAG: Hello. Sorry to be late on
25 the phone. This is Dr. Nag calling in.

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1 CHAIRMAN MALMUD: Thank you, Dr. Nag. We
2 just discussed the infiltration of F-18 FDG
3 therapeutic radiopharmaceuticals. And Dr. Vetter
4 responded that this already had been discussed about
5 10 years ago or so in a publication by Dr. Castronovo,
6 where the infiltrations resulted in, if I am quoting
7 correctly, an even greater radiation burden than these
8 mentioned. Am I correct, Dr. Vetter?

9 VICE CHAIRMAN VETTER: Yes, that is
10 correct. Yes, that's correct.

11 CHAIRMAN MALMUD: And, therefore -- this
12 is Malmud again. And, therefore, the issue really was
13 presented, dealt with, and probably need not be dealt
14 with again. Is that your feeling, Dr. Vetter?

15 VICE CHAIRMAN VETTER: Well, I wouldn't
16 necessarily say it doesn't need to be dealt with, but
17 it has been dealt with in the literature in the past.
18 I don't know if the NRC has ever looked at that
19 literature, but it has been dealt with in the past in
20 the literature, and the doses reported are
21 considerably higher than that particular case that was
22 outlined.

23 So I wouldn't view that particular case as
24 being particularly egregious when compared to what
25 apparently happens routinely in the injection of

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1 radiopharmaceuticals.

2 CHAIRMAN MALMUD: This is Malmud again.
3 Therefore, Dr. Vetter, what would your response be to
4 the question raised by Cindy Flannery? And the
5 question in the last slide is: considering the higher
6 doses from the use of NARM, should NRC change its
7 position to now regard infiltrations as MEs if the
8 resulting dose exceeds the dose limits of 10 CFR
9 35.3045.

10 VICE CHAIRMAN VETTER: My opinion is that
11 the -- that the practice should not be changed at this
12 point in time. However, with the increased use of
13 therapeutic radiopharmaceuticals, I think it is a
14 subject that should be investigated, but nothing
15 changed at this point in time.

16 MEMBER NAG: This is Dr. Nag. My
17 viewpoint would be that this is somewhat akin to the
18 seed migration issue for permanent implant. And that
19 if in the -- if the injection of radioactive material,
20 whether it's 125 ccs or, you know, NARM, if it is
21 routine that some of it infiltrates out, and that this
22 is something that happens in the normal course of a
23 medical event, it should not -- I mean, the normal
24 course of a medical administration, this should not be
25 viewed as a medical event.

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1 CHAIRMAN MALMUD: Thank you, Dr. Nag.

2 Dr. Vetter, do you wish to make your
3 recommendation into a motion?

4 VICE CHAIRMAN VETTER: I would be happy to
5 do that. I move that the ACMUI recommend that the NRC
6 not change its practice regarding the definition of
7 infiltrations as medical events at this time.

8 CHAIRMAN MALMUD: Thank you.

9 Dr. Nag, are you seconding that motion?

10 MEMBER NAG: I will be seconding that
11 motion, but I want to make sure that the following
12 definition says that infiltrations are not medical
13 events. I want to confirm that, please. Can someone
14 confirm that?

15 CHAIRMAN MALMUD: I'll ask -- this is
16 Malmud. I'll ask Dr. Vetter to confirm that in his
17 motion.

18 VICE CHAIRMAN VETTER: Yes, I would accept
19 that as a friendly amendment to the motion. But I
20 think Cindy Flannery can confirm that that is the
21 practice now.

22 CHAIRMAN MALMUD: And I'll ask Cindy, is
23 that the practice now from your view?

24 MS. FLANNERY: Yes. This is Cindy
25 Flannery. Yes, that is NRC's position based on that

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1 supplementary information.

2 CHAIRMAN MALMUD: Thank you, Cindy.
3 Therefore, Dr. Vetter's motion stands, with Dr. Nag's
4 seconding. Is there any discussion of the motion?

5 MEMBER EGGLI: This is Doug Eggli. I'd
6 like to speak to the motion.

7 CHAIRMAN MALMUD: Thank you. Dr. Eggli?

8 MEMBER EGGLI: There are -- infiltrations
9 just always occur. If they were to become medical
10 events, the NRC would be flooded with more medical
11 events than it could manage. But, in addition, the
12 radiation is a function of the volume of distribution.

13 Obviously, the smaller the volume of the infiltration
14 the higher the local radiation dose. In 30 years of
15 clinical practice, I have seen lots and lots and lots
16 of infiltrations. I have never seen an adverse
17 clinical outcome.

18 Unlike non-radioactive iodinated
19 radiographic contrast, which often has significant
20 local complications when infiltrated, I have never
21 seen an adverse outcome from a radiopharmaceutical
22 infiltration in my clinical practice. And I strongly
23 support the motion that they should be left in their
24 current status as not medical events.

25 CHAIRMAN MALMUD: Thank you, Dr. Eggli. I

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1 would second your observation, in that 37 years of
2 nuclear medicine practice I have not seen a negative
3 outcome as a result of an accidental infiltration of a
4 diagnostic radiopharmaceutical.

5 Are there other comments or discussions
6 regarding the motion?

7 MEMBER LIETO: This is Ralph Lieto.

8 CHAIRMAN MALMUD: Yes, Mr. Lieto.

9 MEMBER LIETO: I would also support that
10 the current policy statement of the NRC be maintained.
11 And maybe what we ought to do is just say that we
12 reaffirm it with the, you know, current terminology of
13 replacing misadministration with medical event.

14 The only thing I would maybe suggest in
15 terms of change is that I don't think extravasation is
16 a frequent occurrence in nuclear medicine. Otherwise,
17 you'd have patients being repeated beaucoup times, and
18 it is a very uncommon occurrence. So I would say that
19 we just reaffirm the current statement as it -- that
20 was postulated back in 1980.

21 CHAIRMAN MALMUD: This is Malmud. Mr.
22 Lieto, are you willing to accept and support Dr.
23 Vetter's motion?

24 MEMBER LIETO: Yes, because it basically
25 reaffirms that.

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1 CHAIRMAN MALMUD: Thank you.

2 MEMBER EGGLI: This is Doug Eggli. I'd
3 like to comment again in response to Ralph's last
4 statement.

5 CHAIRMAN MALMUD: Please do.

6 MEMBER EGGLI: I think that complete
7 infiltrations are not as common, although I see them
8 with some regularity, particularly if you have a very
9 young technologist staff. However, partial
10 infiltrations, as a needle flips in and out of a vein,
11 are really quite common and have neither impact on the
12 diagnostic quality of the study, nor long-term adverse
13 impact on the patient.

14 MEMBER LIETO: I accept that
15 clarification.

16 CHAIRMAN MALMUD: Thank you, Mr. Lieto.

17 Any other discussion of the motion on the
18 floor?

19 MR. STABIN: Yes, this is Mike Stabin. I
20 would note that even though this has been treated once
21 or twice in the literature, it is very difficult in
22 these situations to establish what you mean by "the
23 dose." When you're talking about dose to a standard
24 organ, it is pretty easy to define it.

25 But in these cases, as was mentioned by

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1 someone else, it depends on the volume that you
2 assume, the distance from that volume where you assign
3 dose, and so there is not really a good standardized
4 model for people to assign a dose to report.

5 CHAIRMAN MALMUD: Thank you. Are you also
6 supportive of the motion?

7 MR. STABIN: I don't have a position on
8 the motion. I just wanted to contribute that comment,
9 that this would be difficult at the moment I think for
10 people.

11 CHAIRMAN MALMUD: Thank you. I think we
12 all agree with your observation. Are there any other
13 comments?

14 MEMBER FISHER: Dr. Malmud?

15 CHAIRMAN MALMUD: Yes. Who is speaking,
16 please?

17 MEMBER FISHER: This is Darrell Fisher. I
18 would like to follow up on a question raised by Cindy
19 Flannery and ask for your experience and the
20 experience of others, Dr. Eggli in particular. She
21 asked about the case in which a therapeutic
22 administration goes awry in the same way with a high-
23 dose radionuclide such as Yttrium-90, Iodine-131, or
24 even an alpha emitter, when those infusions become
25 more common.

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1 And should the dose be very much greater
2 as a result of an injection of this type? What would
3 be your opinion?

4 CHAIRMAN MALMUD: Are you asking me
5 specifically?

6 MEMBER FISHER: Yes. And Dr. Eggli.

7 CHAIRMAN MALMUD: Thank you. I have not
8 had experience with an infiltration of a therapeutic
9 dose. I have been fortunate in my practice in that
10 the therapeutic doses that we have used have been
11 carefully administered by experienced personnel, and,
12 therefore, the therapeutic doses have not infiltrated.

13 Having said that, I would also comment
14 that Dr. Eggli's observation is a valid one with
15 regard to diagnostic doses, and they not infrequently
16 partially infiltrate.

17 Now, getting back to the question of the
18 therapeutic, the therapeutic may in fact result in a
19 radiation burden which will manifest itself with some
20 visible abnormality. But I have not, fortunately,
21 seen that in my years of practice. The doses we used
22 to use were of pharmaceuticals such as P-32-containing
23 pharmaceuticals.

24 More recently, of course, we are now into
25 other forms of therapeutics, and there is a

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1 theoretical possibility that we will see some untoward
2 effect from an infiltration of a therapeutic dose.
3 However, I cannot personally speak to that experience.

4 Perhaps Dr. Eggli may.

5 MEMBER EGGLI: This is Doug Eggli. I
6 share Leon's good fortune of never having had an
7 intravenous therapy dose infiltrate. Just as a
8 practice, I think our concern here is beta emitters
9 being extravasated in the soft tissue as opposed to --
10 or alpha emitters as opposed to gamma emitters. But
11 we really take a whole different level of care in
12 establishing our IV lines on therapeutic data emitters
13 than you do typically on routine diagnostic studies.

14 And I would think that you will find that
15 the incidence of infiltration of therapeutic beta
16 emitters or other -- or alpha emitters, when they
17 become used, is going to be -- that I think is going
18 to be fairly uncommon because of the quality of the IV
19 that we establish to do that.

20 When you inject a diagnostic
21 radiopharmaceutical, they are often simply done with a
22 straight stick of a needle. And you can perforate the
23 far side of a vein or partially perforate the far side
24 of the vein. If you get a good IV running and you run
25 in 4- or 500 ccs of fluid prior to the administration

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1 of your therapeutic dose, I think the chances that you
2 have a malfunctioning IV are likely to be detected
3 before you administer a therapy dose.

4 And we typically put in a fairly large
5 volume of non-radioactive fluid through an IV where we
6 plan to give a therapy, just to make sure that it
7 really is where we -- a good IV, and that we are not
8 putting anything into the tissues.

9 You can put 10 or 20 ccs of fluid into the
10 tissue and not notice it. It is much harder to put 4-
11 or 500 ccs into the tissue and not notice it.

12 MEMBER NAG: This is Dr. Nag. I agree
13 with you, Dr. Eggli. However, the question would be:
14 if someone is not very conversant with the technique,
15 and is going to be doing an infusion and puts in only
16 20 or 30 ccs, and it is running well, and then start
17 infusing a therapeutic dose, it is possible that it
18 will not extravasate.

19 In that situation, what would the NRC do?
20 I think that's the question that was being asked, or
21 possibly that's a question that would be asked.

22 MEMBER EGGLI: This is Doug Eggli again.
23 Again, I think the incidence of that would be
24 uncommon. And, again, with the therapeutic data
25 emitter, I think it might rise to the level of a

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1 medical event.

2 VICE CHAIRMAN VETTER: This is Dick
3 Vetter. I just wanted to point out a subtle
4 difference in the way diagnostic radiopharmaceuticals
5 are administered versus therapeutic. In diagnostic,
6 they are injected. In therapy, they are infused. And
7 that's a huge difference.

8 As Dr. Eggli mentioned, during infusion it
9 is very carefully -- the IVs are very carefully
10 administered, and then a considerable amount of saline
11 is used to make sure you have a patent IV. And some
12 medical centers, even during the administration of the
13 therapeutic radiopharmaceutical, will periodically
14 interrupt the administration and administer some
15 saline to make sure that the line continues to remain
16 free.

17 So it is really two different -- totally
18 different types of injection or administration.

19 MEMBER SULEIMAN: Yes. This is Orhan.
20 Are we in fact discussing the therapeutic? I thought
21 the question was really limited to the diagnostic. I
22 have no trouble discussing the therapeutic, but does
23 the NRC want it answered? And have we digressed?

24 CHAIRMAN MALMUD: Orhan, this is Malmud
25 again. You are correct. The motion referred to the

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1 diagnostic. And if you wish to -- if there is an
2 interest in discussing the therapeutic, I think that
3 we can, but it might be best to first achieve closure
4 on the diagnostic.

5 Are there any other comments regarding the
6 diagnostic?

7 (No response.)

8 If not, may we move the motion forward?
9 All in favor of the motion?

10 (Chorus of ayes.)

11 Are there any opposed to the motion?

12 (No response.)

13 Are there any abstentions?

14 (No response.)

15 Thank you. Therefore, the motion is
16 approved unanimously regarding the infiltration of
17 diagnostic radiopharmaceuticals.

18 We are getting static again. Could some
19 -- those who are not talking -- thank you. Thank you.

20 The discussion regarding therapeutic
21 radiopharmaceuticals I think was well summarized in
22 the comments made by several of you. It is the
23 practice in administering therapeutic
24 radiopharmaceuticals to first establish an intravenous
25 line, and to make certain of its patency.

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1 And that differs from the injection of a
2 diagnostic radiopharmaceutical, which is, as correctly
3 described, an intravenous injection without the prior
4 establishment -- most often without the prior
5 establishment of an intravenous line.

6 Now, therefore, a question arises, and
7 that is this is a -- first, a statement. It is a
8 common practice for us medically to establish an
9 intravenous line or therapeutic doses that are given
10 IV. Should this be a matter of written requirement
11 that -- and, quite frankly, I am not certain if it
12 already is or is not. Is anyone familiar with the
13 regulations regarding the administration of
14 therapeutic radiopharmaceuticals? Do we require an
15 intravenous line?

16 MEMBER LIETO: The regulations do not.

17 CHAIRMAN MALMUD: Should they?

18 MEMBER LIETO: This is Ralph Lieto. I
19 don't think we should enter into the practice, since
20 things might change regarding that. I think the less
21 we have in the regulations the better.

22 CHAIRMAN MALMUD: Thank you.

23 MEMBER SULEIMAN: This is Orhan. I would
24 agree with Ralph. I mean, the route of administration
25 may vary depending on the pathology, and so limiting

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1 it to one way of administering is going to cause
2 problems.

3 CHAIRMAN MALMUD: Thank you. Are there
4 any other opinions regarding that issue?

5 VICE CHAIRMAN VETTER: This is Dick
6 Vetter. I agree with that as well. And, in fact, I
7 am sure that the method of administration was worked
8 out during development of the protocol. So it is
9 probably already in the FDA literature on how the
10 material should be administered.

11 CHAIRMAN MALMUD: Thank you. So with
12 those opinions, we will lay the issue of the
13 therapeutic radiopharmaceuticals to rest at the
14 moment, and move on with the rest of our agenda, if
15 that is agreeable with the participants in today's
16 discussion.

17 MEMBER NAG: Yes, that is agreeable.

18 CHAIRMAN MALMUD: Thank you.

19 MS. FLANNERY: Dr. Malmud, this is Cindy
20 Flannery.

21 CHAIRMAN MALMUD: Yes, Cindy.

22 MS. FLANNERY: I think we are also trying
23 to get some input or feedback on how this applies to
24 therapeutics. And I do want to just add one thing, a
25 comment that Dr. Vetter made, that, you know, your

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1 therapeutic administrations are infused. And in this
2 particular case, this F-18 was handled the same way.
3 It was described at a 10 mL flush, and a 100 mL
4 infusion was done prior to the injection.

5 So I understand that even when you have a
6 line set up like that, to prevent it from happening,
7 realize that it is incredibly rare, but as in this
8 case there is that potential. So we would like to get
9 some input on how this would apply to therapeutic
10 administrations.

11 CHAIRMAN MALMUD: Thank you. May we have
12 some opinions regarding how this should be ideally
13 worded?

14 MEMBER EGGLI: This is Doug Eggli. Even
15 though it was given through an IV line, and we give
16 all of our PET doses through an IV line, there are IV
17 lines and there are IV lines, and there are levels of
18 care taken in establishment of the IV line that I,
19 again, think are really quite different in therapeutic
20 and diagnostic.

21 The quality of the needle catheter used, a
22 butterfly versus an angiocath or some other form of
23 internal catheter makes a great deal of difference in
24 the quality of the line and the likelihood of an
25 infiltration. So, again, I think that the likelihood

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1 in a therapeutic infusion is really very small.

2 However, we are infusing currently often
3 beta emitters, and I am less concerned with gamma
4 emitters than I am with the local radiation with beta
5 emitters. And if we infuse and infiltrate a beta
6 emitter in large quantities, it is conceivable we
7 could see tissue damage.

8 I am not as -- I am not opposed to making
9 a therapeutic infiltration of medical event, but I
10 think it probably requires some more discussion about
11 things I am probably not thinking about. But, again,
12 I think it will be uncommon. And, again, let me say
13 that not all IV lines are the same.

14 MEMBER NAG: This is Dr. Nag. The problem
15 is that, how will you define -- for example, in other
16 areas we say if it is more than 20 percent, you know,
17 we have a number like 20 percent dose, how can you say
18 that -- you know, how much infiltration? Like if one
19 is infiltrated, obviously, that is not going to be a
20 medical event. If the whole dose is infiltrated, I
21 mean, that obviously would be a medical event. So how
22 would you say how much of it infiltrated in terms of
23 quantity? And that may be a difficult thing. It may
24 need a separate discussion.

25 MEMBER EGGLI: This is Doug Eggli. I

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1 agree with you on that, Subir. But I think, again,
2 the flag would probably be a function of local tissue
3 exposure, and is there enough local radiation
4 deposited that acute tissue injury is likely to occur.

5 MEMBER NAG: Again, that would be very
6 hard to quantitate.

7 CHAIRMAN MALMUD: Gentlemen, may I ask if
8 it would be an issue which we should bring to the
9 ACMUI and discuss with regard to which type of
10 material should be used for infusions of beta-emitting
11 therapeutic pharmaceuticals, radiopharmaceuticals, so
12 that we can discuss it at length.

13 I think the point that was made about a
14 butterfly versus an intravascular catheter is
15 relevant, because butterflies can infiltrate easily,
16 particularly when there is arm movement by the
17 patient. And whereas intra-caths, once established,
18 of one type or another, generally are less likely to
19 perforate the vessel.

20 So that this is an issue which may be
21 worth discussing at the -- as an agenda item at the
22 next ACMUI. Therefore, I am making a recommendation
23 that it be discussed at the next ACMUI rather than
24 attempting to resolve it on a conference call without
25 having a chance to have thought it through with all of

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1 its ramifications. Is that acceptable to the
2 committee?

3 MEMBER NAG: I would agree -- I would
4 support that wholeheartedly.

5 MEMBER EGGLI: This is Doug Eggli. I
6 agree.

7 CHAIRMAN MALMUD: Is there anyone that
8 doesn't agree?

9 MEMBER SULEIMAN: This is Orhan. I would
10 agree, but I think it's a much more complicated issue,
11 and I am even hesitant to bring it up without more
12 preparation, because somebody mentioned beta emitters
13 versus gamma. I think you have to look and see that
14 at some point you may see alpha emitters being
15 approved in the U.S. And we are not talking about
16 diagnostic here, we are talking about therapeutic and
17 the optimum administration.

18 So it is very, very fuzzy to me, you know,
19 where the -- where the practice of medicine and
20 specific protocols come into play, and where the
21 radiation dose excesses or events would come into
22 play. So I think we should discuss it, but I am
23 nervous about bringing it up without adequate
24 preparation. Otherwise, the discussions could be in a
25 very circuitous, neverending kind of mode.

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1 CHAIRMAN MALMUD: Orhan, I think you are
2 right, but it points out once again the complexity of
3 the issue, and, therefore, the fact that this
4 important subject brought up by Cindy is better dealt
5 with in a meeting of the ACMUI than on a conference
6 call such as this.

7 MEMBER SULEIMAN: I agree.

8 CHAIRMAN MALMUD: Is there anyone who was
9 opposed to delaying this to the next meeting of the
10 ACMUI?

11 MEMBER GILLEY: This is Debbie. I am not
12 opposed. I just wanted you to know I am on the call.

13 CHAIRMAN MALMUD: Thank you, Debbie. We
14 are glad that you are on the call.

15 Therefore, recognizing that it is a
16 potentially important issue, we will ask that it be
17 included on the agenda for the next ACMUI. The result
18 of the next ACMUI meeting may be that we will
19 establish a subcommittee to look at it, because of its
20 complexity. On the other hand, given the fact that it
21 is brought to our attention today, it seems to me that
22 we should bring it to the next ACMUI, so that we keep
23 it on the agenda and deal with it as promptly as
24 possible.

25 If that is acceptable with the committee,

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1 we will do that. If not, we will do whatever the
2 committee recommends instead. Is it acceptable to the
3 committee members?

4 (Several members respond in the affirmative.)

5 Thank you. Then, Debbie and Cindy, do we
6 have any other items to discuss on today's agenda?

7 MS. FLANNERY: Yes, we have one more
8 agenda item.

9 CHAIRMAN MALMUD: And Dr. Vetter? Dr.
10 Vetter? Dick? Dr. Vetter? Is Dr. Vetter with us?

11 VICE CHAIRMAN VETTER: Am I with you now?
12 I guess my mute was on.

13 CHAIRMAN MALMUD: Dick, I have to give a
14 therapeutic dose right now. I am going to run out for
15 five minutes and come back, so --

16 VICE CHAIRMAN VETTER: Okay.

17 CHAIRMAN MALMUD: -- could you take over
18 for me?

19 VICE CHAIRMAN VETTER: As long as you make
20 sure that that line is well administered, yes.

21 CHAIRMAN MALMUD: It's an oral dose,
22 and --

23 VICE CHAIRMAN VETTER: Oh, it's an oral.
24 Okay.

25 CHAIRMAN MALMUD: -- the practice of my

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1 department is that I do it personally. So just give
2 me five minutes and I will be back.

3 VICE CHAIRMAN VETTER: Okay. I will be
4 happy to chair the meeting while you are gone.

5 CHAIRMAN MALMUD: Thank you.

6 VICE CHAIRMAN VETTER: So did he try to
7 give the floor back to Cindy for the next item on the
8 agenda?

9 MS. FLANNERY: Yes. I can open up that
10 one as well. Okay. The next topic is on the
11 NeoVista's device. We discussed it at the October
12 meeting. And just to kind of give a little bit of
13 background information, the current licensing guidance
14 for the use of NeoVista's EpiRad ophthalmic device
15 requires an authorized user to meet the T&E
16 requirements in either 35.490 or 10 CFR 35.690, which
17 essentially means that an AU must be a radiation
18 oncologist.

19 Now, at the October ACMUI meeting, a
20 recommendation was made to revise the licensing
21 guidance to allow for the training and experience
22 requirement in 10 CFR 35.491, accompanied by
23 appropriate device-specific training to be adequate
24 for an AU for the EpiRad device.

25 Now, 10 CFR 35.491 allows physicians to be

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1 an AU with only 24 hours of classroom and laboratory
2 training applicable to the medical use of Strontium-90
3 for ophthalmic radiotherapy, along with supervised
4 case experience of five clinical treatments.

5 While this may be adequate for the
6 standard treatments of 24 Gray of a single lesion for
7 the treatment of age-related macular degeneration, as
8 used in the clinical trials, NRC staff's concern is
9 whether this would be adequate for off-label use.
10 Now, once the device is FDA approved, it is perfectly
11 legal to use the device using protocols different than
12 the protocol followed under the clinical trials.

13 And it is also worth noting that just last
14 week FDA granted a waiver to treat a patient who did
15 not meet the criteria for inclusion in the current
16 investigational treatment protocol. So what we would
17 like today is just to get some input from ACMUI on
18 whether their previous recommendation from October's
19 meeting should apply to both the use in the clinical
20 studies as well as to the off-label use once this
21 device gets FDA approved. If not, NRC staff hopes to
22 receive ACMUI's recommendation on what would be
23 adequate training and experience for off-label use.

24 And I guess another consideration is
25 whether we should have two different categories of

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1 qualifications for authorized use in the licensing
2 guidance. For example, having one for the standard
3 use of 24 Gray for the treatment of AMD, as used in
4 the clinical trials, and maybe another set of
5 qualifications for off-label use.

6 So that is all I really had for opening up
7 this discussion.

8 Thank you.

9 MEMBER NAG: Hi. This is --

10 VICE CHAIRMAN VETTER: Thank you, Cindy.
11 the floor is open.

12 DR. HEIER: I would like to acknowledge
13 that -- my name is Jeff Heier, and I spoke at the
14 previous meeting. And I am on as a clinical
15 investigator with the EpiRad 90 device.

16 MEMBER EGGLI: Okay. Dick, this is Doug
17 Eggli.

18 VICE CHAIRMAN VETTER: Go ahead, Doug.

19 MEMBER EGGLI: I think I made the motion,
20 so let me speak to my intent for that motion, which
21 was to specify the training and experience only for
22 the standard therapy as described in the protocol, not
23 for any more extended therapy where dosimetric
24 considerations may become very important.

25 So I think the motion, as we passed it,

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1 was intended only for the standard treatment and not
2 for anything beyond that.

3 VICE CHAIRMAN VETTER: Thank you. Dr Nag?

4 MEMBER NAG: Yes, this is Dr. Nag. I have
5 quite strong feelings on this. Firstly, I think at
6 the last meeting one of the other radiation
7 oncologists, Jim Welsh, was not there. I mean, he had
8 to leave. He had very strong feelings, and I believe
9 he has sent an e-mail to all of the ACMUI and NRC, you
10 know, on this yesterday. So I think those views have
11 to be taken into account.

12 The fact that neither Jim Welsh was there,
13 nor the Chairman of the ACMUI was there at the meeting
14 at the time of the voting, would have to be taken into
15 account, and I think we should revisit this.

16 The major concerns that we have are: a)
17 although this is right now being used as a learning
18 tool, once it is FDA approved it can be used for off-
19 label and any other uses. For those things, you do
20 need a radiation oncologist to be on the Planning
21 Committee. The major objection that was made was
22 that, you know, it makes it difficult to have a
23 radiation oncologist onsite.

24 However, we are not saying that there is
25 the physical presence of the radiation oncologist

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1 needed. We are saying that the radiation oncology and
2 the radiation physicist has to be part of the team,
3 not necessarily to be onsite. So, therefore, to get
4 the program going, this can be gotten going as a team,
5 and it will not delay any treatment, because the
6 radiation oncologist is not onsite.

7 Secondly, when NeoVista presented this to
8 the CMS for approval, they said that the procedure
9 will be done with the ophthalmologist in conjunction
10 with the radiation oncologist and radiation physicist.

11 And, therefore, the code for the procedure was made
12 with this complex situation in mind, and, therefore,
13 it reimbursed at the higher rate.

14 If you now bypass this, then basically you
15 are doing a Medicare fraud, because you are now going
16 to charge the higher level for doing something at the
17 much lower level. So these are all considerations
18 that need to be discussed very carefully before we
19 have a vote.

20 And I would very much like the people who
21 have the most knowledge about this, which is the two
22 radiation oncologists on the panel, plus the radiation
23 medical physicist, the medical -- the radiation
24 oncology medical physicist to be on when any vote is
25 taken, because they have the most expertise on what

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1 are the negative and what are the problems associated
2 with radiation at the high dose in a localized area.

3 VICE CHAIRMAN VETTER: Dr. Thomadsen, did
4 you want to make any comments on this issue?

5 MEMBER THOMADSEN: I would second
6 everything that Subir just said. I am very concerned
7 that this type of therapy would be going on without
8 the input of somebody who has grown up in radiation
9 oncology and understands the radiation. And while the
10 results of the trial may be positive, may show very
11 good results at the dose level selected, once people
12 start looking at that they very likely are going to
13 try to find other dose levels.

14 Once authorization has been given to the
15 retinal surgeons to be authorized users, they will be
16 in charge of that. They won't be using the radiation
17 oncologists as resources during that procedure of dose
18 investigation. And that is probably not good for
19 patients.

20 VICE CHAIRMAN VETTER: Dr. Heier, did I
21 hear you request to --

22 DR. HEIER: Yes, I did, if I could make a
23 comment. I certainly understand those concerns. They
24 are -- I think it's very important to understand that,
25 at least as a retina specialist, and a busy retina

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1 specialist who treats this disease, probably to the
2 tune of 20 to 30 patients a day, the intention of the
3 way this study was designed, and absolutely the
4 intention of how we intend to use this, is if this --
5 if the Phase 3 study or the pivotal studies replicate
6 the results we have seen in the Phase 2 studies, this
7 will be administered as a single dose in a dose that
8 was determined in collaboration with radiation
9 oncology and with the radiation physicist.

10 If it turns out that this treatment, as
11 described this way, cannot be delivered in that
12 manner, I completely agree that this is a whole
13 different process and should be looked at completely
14 differently, and, quite frankly, probably is not going
15 to be applicable to the treatment for most people with
16 this disease, because the numbers we see with this,
17 our approach to it, and the frequency we have to treat
18 it, it is not going to make that type of approach
19 practical.

20 And so as it has been explained here, and
21 as I use it in the clinical trials, and as everybody
22 else does, we are looking at it in a very planned,
23 finite approach. And if the studies don't demonstrate
24 that that approach is practical, then it needs to be
25 completely reevaluated.

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1 And whether or not, in collaboration with
2 radiation oncology, that can be determined in a way
3 that is appropriate is a whole other saying. And I
4 know personally that is not an approach that I would
5 be -- I would be applying to my patients, just on the
6 sheer numbers and the complexity of what we have to do
7 already.

8 As it is right now, all of the
9 determinants in the process are determinations that
10 are made, the type of neovascularization, the size of
11 it, and the surgical approach how the probe is laid,
12 and these are similar approaches that we do in
13 determining our laser therapies, in determining our
14 surgical approaches to patients.

15 The input is entirely done from a retina
16 specialist standard. If all of that has to be
17 modified, I completely agree this has to be
18 reevaluated. But it is going to completely change how
19 this therapy may or can be delivered.

20 MEMBER NAG: Hi. This is Dr. Nag. We
21 have inquired within the radiation oncology community.

22 There are not that many places that are doing
23 NeoVista, but the places that are doing NeoVista do
24 have the collaboration of the radiation oncologists.
25 That does not mean that the patients held up until the

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1 radiation oncologist can get to the OR.

2 No. That -- the whole planning team is
3 part of the planning team. So this -- having a
4 radiation oncologist be part of the team does not hold
5 up any patient. You could be doing 20 patients per
6 day; that doesn't mean that the radiation oncologist
7 is going to be there during -- for all the 20
8 patients. It means that the program, the radiation
9 safety program, is under the supervision umbrella of a
10 radiation oncologist.

11 So this -- I would like to emphasize
12 having a radiation oncologist on the team only helps
13 in the safety. It does not hamper the access to any
14 patient, because you don't have to wait for a
15 radiation oncologist to say yes before you go ahead
16 with one single procedure.

17 DR. HEIER: So, Doctor, I guess I'm a
18 little confused then, because this is -- I have done
19 other radiation trials as well for AMD, and, in fact,
20 they were impractical. The way this study works,
21 there is -- the input from the radiation oncologist
22 has already been determined. So the input from the
23 radiation oncologist has already been determined, and
24 the approach doesn't change from the radiation
25 standpoint for any of the patients.

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1 So right now I guess I am not sure we have
2 a radiation safety officer involved for the handling
3 of the radiation and the storage of the radiation. So
4 I see there are two arguments. One, the argument at
5 the committee meeting was we are probably not treating
6 patients in the best available manner if some of them
7 would not benefit from alterations of either the
8 amount or the approach of the radiation delivered.
9 And that may or may not be the case, but, if that is
10 the case, that is the type of scenario that becomes
11 very impractical.

12 If the way it is right now, where at the
13 other sites if there is no delay, then I think that is
14 because right now there is no input. All of the
15 approach has already been determined, so any of the
16 different factors per patient are solely determined by
17 the retina specialist.

18 VICE CHAIRMAN VETTER: Do any other
19 members of the committee wish to speak to this issue?

20 MEMBER FISHER: Dr. Vetter, this is
21 Darrell Fisher. A question for Dr. Nag. In an active
22 clinical setting, where the ophthalmologist is
23 treating 20 to 30 patients a day, what is the
24 contribution of the radiation oncologist?

25 MEMBER NAG: The contribution of the

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1 radiation oncologist would be --

2 MEMBER FISHER: But to the individual
3 patient --

4 MEMBER NAG: Not to the individual
5 patient, to the overall program. It is to make sure
6 that the program is set properly, that the dose
7 levels, and so forth, are set properly. And if
8 individual patients do come in that require
9 modification as the program goes on, there will be
10 someone to monitor, so that the modification, if
11 needed, will be required.

12 So you don't need to call in that
13 radiation oncologist for every patient, but to set up
14 the program itself.

15 MEMBER FISHER: What is the modification
16 that would require intervention by a radiation
17 oncologist in a procedure for wet AMD?

18 MEMBER NAG: Okay. The problem is unless
19 you go into the -- you know, in almost any treatment
20 you always have to modify things as they go on,
21 depending on the response you are seeing. Do we need
22 to change the dose? Do we need to change, instead of
23 a single-point application, maybe a two-point
24 application? Do we need to change the direction?

25 So those kinds of modifications are

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1 possible. And if you set this that it can only be
2 done one way, you are not going to be addressing it
3 and possibly making things better if need be. You are
4 now -- your hands are tied, because you can only do it
5 one way.

6 MEMBER FISHER: But doesn't the retinal
7 ophthalmologist performing this procedure have more
8 knowledge and experience than your radiation
9 oncologist?

10 MEMBER NAG: The retinal specialist has
11 more knowledge and experience on eye. They do not
12 have knowledge and experience on radiation dosimetry
13 and radiation microdosimetry. How do radiation may --
14 millimeters, how do radiation doses change depending
15 on the angulation? Those minute things are what
16 sometimes makes a huge difference.

17 I can give you an analogy on cardiac
18 brachytherapy, which is in the domain of the cardiac
19 surgeon or the cardiologist, because they know most
20 about the heart, they know most about the cardiac
21 vessels. When they did their experiment initially
22 without much input from radiation oncologists, they
23 were seeing a large number of failures at the end.

24 And when the radiation oncologist went
25 into detail, they found this is due to the impact,

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1 and, you know, you have to prolong the length and you
2 have to modify the dose distribution. So unless you
3 have those inputs, you are not going to advance this.

4 And, basically, you are sort of -- you are
5 preventing this from going further, and, you know, you
6 are now at the standpoint that you can only do 24
7 Gray. At that point, you cannot do any improvements
8 to that. And, you know, are you getting the -- let's
9 say you get a 70 percent success rate. Would you get
10 80 or 90 percent success rate if you changed some of
11 the parameters, some of the angles?

12 Those are questions that will be
13 unanswered if you tie yourself with only one dose, one
14 parameter. You know, I would have liked my colleague,
15 Jim Welsh, to have given his input, but I have talked
16 with him and basically he has very similar concerns.
17 I don't know if Dr. Thomadsen has, you know, any
18 concerns along these lines.

19 MEMBER SULEIMAN: Well, I have already
20 expressed that I do, indeed. I think it is a very bad
21 idea to try to take the radiation oncologist out of
22 the loop. We have already said that the radiation
23 oncologist does not have to be there when the
24 procedure is being done, so coordination becomes
25 simpler from the retinal surgeon's point of view.

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1 Certainly, in the procedure room, the
2 medical physicist or radiation safety officer should
3 be there to handle any radiation emergency that could
4 happen. And that coordination still would have to be
5 done, no matter what was going on here.

6 But I think the -- having the radiation
7 oncologist involved is essential, whether or not you
8 need to have each patient seen by the radiation
9 oncologist. If the patient is just on a clinical
10 trial, I think that is questionable. Any patients off
11 the clinical trial start presenting big problems.

12 VICE CHAIRMAN VETTER: This is Dick
13 Vetter. If I could just ask Cindy Flannery to get us
14 back to square one here and clarify what the committee
15 approved in October. I believe it was to apply the
16 training specified in 35.491 to the 24 Gray standard
17 procedure, standard treatment. And that was the only
18 thing it applied to.

19 From the discussion here, it sounds like
20 the committee would have a problem expanding the
21 procedure to off-label use or which I guess it was a
22 two-point treatment. But just to be clear, the only
23 -- I think -- if Ms. Flannery could confirm for us --
24 the only thing we approved was the application of
25 35.491 to the standard procedure.

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1 MS. FLANNERY: I don't think that's
2 correct. I think the recommendation that was made is
3 that the training and experience requirements in 491
4 would be adequate to be an authorized user for this
5 new device. It didn't limit it to just the use in the
6 clinical trial, so that --

7 VICE CHAIRMAN VETTER: Okay. That --

8 MS. FLANNERY: -- is a question to you is,
9 you know, this recommendation that ACMUI made, is that
10 applicable to off-label use as well? Because that --
11 you know, it wasn't specified in the recommendations.

12 MEMBER NAG: This is Dr. Nag.

13 MEMBER EGGLI: This is Doug Eggli again.
14 I made that motion. And I know what the intent of the
15 motion was, and the intent was to the simple 24 Gray
16 procedure, on-label use only.

17 MEMBER NAG: This is Dr. Nag. I do
18 remember that day, it was getting towards the end of
19 the day, and end of the meeting. I felt that there
20 was inadequate time for discussion, but the motion was
21 called, and, therefore, voted upon. And I believe it
22 was somewhat premature to have taken the vote, but,
23 anyway, that was done. I believe we really need to
24 think this a little more thoroughly.

25 Some of the people who are directly

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1 involved, which would have included Dr. Welsh as one
2 of the radiation oncologists, was not present. The
3 Chairman of the ACMUI was not present. And I think
4 this does require more thinking before we, you know,
5 give a blank check.

6 MEMBER LIETO: Dr. Vetter?

7 VICE CHAIRMAN VETTER: Yes.

8 MEMBER LIETO: This is Ralph Lieto. First
9 of all, a point of clarification. Dr. Welsh was
10 there. If you look at the minutes on October 28th, he
11 did make a number of comments, and Dr. Nag has echoed
12 I think nearly all of those concerns that Dr. Welsh
13 expressed at the meeting.

14 MEMBER NAG: Actually, Dr. Welsh was not
15 present during the voting.

16 MEMBER LIETO: Excuse me. Point of order.
17 Excuse me. The one thing that I would also like to
18 -- I would agree with Dr. Eggli in that the
19 presentation, and I think that the manner in which the
20 vote was taken, was that the training and experience
21 requirements were based on the fact of the
22 presentation that this was a fixed dosimetry -- in
23 other words, 24 Gray at the center, and I think it was
24 6 Gray, or something like that, out to a perimeter of
25 five and a half millimeters.

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1 The second point was that this was a fixed
2 -- a visually identified location by the retinal
3 specialist, so there was visual confirmation of the
4 treatment site by the retinal specialist. And that
5 there was -- this was a single site treatment per
6 application.

7 And so I think all of those things were I
8 think the predicate for the vote that was taken and
9 the motion made by Dr. Eggli. At least that was my
10 interpretation at the time.

11 I think, based on some of the concerns
12 raised here, that since this is not -- this is a 1,000
13 -- or, actually, not a 1,000, but in terms of
14 regulatory guidance for this, we might want to think
15 about adding as a part of the regulatory guidance for
16 this application that the authorized user training and
17 experience requirements are the same regardless of
18 off-label versus labeled use; two, that an AU with
19 35.400 approval is on the license.

20 So that you would have to have the -- that
21 type of training and experience available, and that a
22 person that needs to be present in addition to the --
23 say, the retinal specialist is the RSO or his
24 designee.

25 CHAIRMAN MALMUD: This is Malmud. I've

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1 been listening back on the committee with you again.

2 Mr. Lieto, is that a motion?

3 MEMBER LIETO: Before I make it a motion,
4 I just would like to have it discussed as possible.
5 Or does it have to be a motion to be discussed?

6 MEMBER NAG: I think we can have a
7 discussion -- I think this does require more
8 discussion before we can crystallize it into a motion.

9 DR. HEIER: I'm sorry. This is Dr. Heier
10 again. I would also just like to point out that all
11 of the potential changes are by no means changes that
12 have been put forward by the users of the NeoVista
13 device. From a retina specialist standpoint, the
14 intention is exactly as it was proposed before. This
15 is a single dose, single site treatment, and, in fact,
16 if the pivotal study does not demonstrate the efficacy
17 of this, that is an issue for the treatment overall.
18 There are no intentions on the clinical investigator's
19 part to modify this in any way.

20 MEMBER LIETO: Thank you for clarifying
21 that, Malmud.

22 MEMBER NAG: This is Dr. Nag.

23 MEMBER THOMADSEN: This is Thomadsen.

24 CHAIRMAN MALMUD: Yes.

25 MEMBER THOMADSEN: And I think that is one

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1 of the problems, that if there were a successful trial
2 here, assuming that you don't cure 100 percent of the
3 patients in that trial, the next step of course would
4 be to investigate what you could do to improve that.
5 That is sort of the nature of most radiotherapy
6 regimes.

7 The fact that the -- that it is being said
8 now that that would not be part of the thought, I
9 think is either disingenuous or narrow-sighted.

10 DR. HEIER: That would be the focus of
11 another study. That would then have to go through the
12 same types of parameters and criteria that this one
13 has. I mean, it has been my experience that if we
14 look to modify a procedure, we then need to go through
15 all of the steps to do that. And especially with
16 devices such as this, there are very appropriate
17 critical steps you have to do in order to have that go
18 through a study.

19 MEMBER SULEIMAN: This is Orhan. This is
20 Orhan Suleiman. First off, I want to clarify that
21 once a protocol or a medical product has been cleared
22 or approved by FDA, how it is used by the medical
23 physician is really up to them. So you're getting
24 under this practice of medicine issue.

25 They can -- if they think it is in their

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1 professional judgment that if they change the dose
2 they change a dose, they modify the protocol in any
3 way that they think is medically necessary, they can't
4 do that. The issue that I see -- and I'll ask the NRC
5 staff to step in -- is when does the radiation safety
6 aspect that is the responsibility of the NRC come into
7 play in terms of they may be deviating the medical
8 process, but, in fact, are we now introducing a very,
9 very different radiation safety issue that needs to be
10 addressed?

11 So I don't want anybody to assume that
12 just because it has been approved in a very specific
13 way, with a specific protocol, that that is
14 necessarily how it is going to be practiced out there.

15 And if it is changed, it may be because of other
16 trials, it may be very well because of the
17 individual's position or practice. They want to --
18 it is their prerogative to make some minor -- what
19 they would perceive as minor but maybe better
20 adjustments in the protocol.

21 MEMBER NAG: This is Dr. Nag. You know,
22 the issue was raised that if this does not work, there
23 would be a new policy made. Where would you get the
24 input if the radiation oncologist has not made the
25 input now? They need to get -- they need to know what

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1 are the problems that are occurring. Maybe the wrong
2 angle, maybe it is the positioning. So all of these
3 little things are known only when you are in the OR.

4 I used to do a lot of eye plaque. We
5 modified a lot of eye plaque based on what I saw in
6 the OR. I am not an ophthalmologist. But when I go
7 to the OR, I see what the ophthalmologist is doing. I
8 learn from them, and I give feedback to them. So the
9 feedback cycle is very, very important.

10 DR. HEIER: Doctor, this is a totally
11 different procedure. You won't have a view of this.
12 This is done through the operating microscope, and the
13 only other person who will be there is an
14 ophthalmology surgical trained assistant. So you
15 won't have a view of this. If you have a view through
16 the monitor, it doesn't give you 3-D. It won't give
17 you any of the type of input you are talking about
18 that would enable you to make modifications.

19 If this -- there is -- at least in my
20 circles, there is no intent of redesigning the
21 protocol if this does not work. I understand that
22 this may not be the ideal approach from a radiation
23 oncology standpoint, but this is a very practical
24 approach to 200,000 new cases of wet AMD we see every
25 year, and two million patients with this.

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1 There is a practical component here that
2 we have to deal with. And if that changes, there is
3 no intent of this going further.

4 MEMBER NAG: This is Dr. Nag. If, for
5 example, you get a 70 percent response, and if there
6 was a way to get a 90 percent response, would you want
7 to deprive your patients from going from that 70
8 percent to 90 percent, because you said there is only
9 one way of doing it? This is the dose I chose at
10 random, and this is the dose I am going to go forever.
11 If you can improve it, why not?

12 DR. HEIER: I understand. But I fail to
13 see how radiation oncology will modify that from the
14 basis of this procedure. We've got fluorescein
15 angiograms that take us two years of fellowship to
16 truly appreciate and read. We have the surgery which
17 is being done, which goes through a two-year
18 fellowship, which you are not going to be able to look
19 at directly.

20 So it is -- I am not questioning the skill
21 of the radiation oncologist in modifying that. Some
22 of the intricacies and difficulty of the whole process
23 is how this is applied and the manner in which it is
24 applied and how to interpret that. And right now the
25 only means we have of interpreting that are with the

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1 retinal techniques and diagnostics that we have.

2 And that requires -- does that mean the
3 radiation oncologist is going to go through a two-year
4 fellowship to enable him to interpret the angiograms
5 and be involved in the surgical assist, so that we can
6 eliminate the surgical assist, so he can have the
7 view?

8 MEMBER NAG: We can ask the same question.

9 Do you want to go through a four- or five-year
10 radiation oncology training to know all of the nitty-
11 gritty details of radiation oncology and how the
12 microdosimetry is presented? So this is a
13 collaborative effort, and you need the skills of both,
14 and you are depriving your patients right now of the
15 skills of one.

16 The second point is that when this was
17 presented to the CMS, the CMS approved this and gave
18 us codes, the complexity of which was due to the
19 coordination that NeoVista said this would be done
20 under collaboration with the ophthalmologists and the
21 radiation oncologists and radiation physicists. And
22 now, you know, they are going back on their word to
23 the CMS.

24 DR. HEIER: So I would defer. I am not
25 privy to those discussions. I wasn't involved with

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1 them. I would defer those discussion to NeoVista.

2 MEMBER NAG: Okay.

3 CHAIRMAN MALMUD: Gentlemen, have you all
4 had an opportunity also to read Jim Welsh's e-mail
5 regarding this issue?

6 (Several members respond in the affirmative.)

7 Thank you. So it doesn't need to be read
8 into the minutes?

9 MEMBER NAG: It could be an attachment to
10 the minutes.

11 CHAIRMAN MALMUD: I will put it as an
12 attachment, if you have all had the opportunity to
13 read it. Yes, it will be an attachment to the
14 minutes.

15 Okay. Thank you.

16 Now, let me get back on track. And the
17 question on the table is training and experience
18 requirements for the medical use of the material. And
19 do we have any kind of a motion from a member of the
20 committee regarding such?

21 MEMBER NAG: This is Dr. Nag. I would
22 like to formulate the motion.

23 CHAIRMAN MALMUD: I think I heard Cindy's
24 voice?

25 DR. HOWE: No, this is Dr. Howe. Just

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1 before you make a motion, I wanted to clarify that
2 during the last ACMUI meeting I asked for a
3 clarification as to whether the AU had to be a retinal
4 surgeon, and the ACMUI voted no, it is just a
5 physician. So I want the ACMUI to remember that we
6 have not designated the AU as someone with retinal
7 specialty.

8 CHAIRMAN MALMUD: Thank you for reminding
9 us of that.

10 DR. HEIER: I'm sorry, this is -- the
11 reason that wasn't designated, it was felt that nobody
12 would be going in to do a peritectomy who wasn't a
13 retinal specialist.

14 CHAIRMAN MALMUD: Thank you.

15 DR. ZELAC: Dr. Malmud?

16 CHAIRMAN MALMUD: Yes. Who is speaking?

17 DR. ZELAC: This is Ron Zelac.

18 CHAIRMAN MALMUD: Thank you, Dr. Zelac.

19 DR. ZELAC: If you can indulge me, I would
20 like to just make a brief statement.

21 CHAIRMAN MALMUD: Please do.

22 DR. ZELAC: Clearly, I think everyone
23 understands that patient safety is an NRC concern.
24 That is the first point. Secondly, the principal
25 approach that is used by NRC is through assuring that

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1 the patient gets what the physician wanted. That is
2 as far into medical practice as we go.

3 But the decision on what is needed is in
4 fact the physician's. Therefore, NRC relies on having
5 qualified physicians, qualified on the basis of their
6 training and experience requirements being met.
7 Approvals are not protocol-specific, but they are use-
8 specific. An AU is an AU, and can do what he or she
9 wants. So modifications of the protocol are within
10 the scope of the authorization.

11 Therefore, it behooves us, as regulators,
12 to be sure that the qualifications of those who are
13 approved as authorized for a particular purpose indeed
14 are appropriately qualified to do the variety of
15 things which are available once that authorization is
16 granted.

17 MEMBER NAG: Could you repeat that last
18 portion, Dr. Zelac?

19 DR. ZELAC: I'll try.

20 MEMBER NAG: Or clarify, basically.

21 DR. ZELAC: What I was trying to put
22 across is the point that once an individual has met
23 the training and experience requirements, and is
24 designated as an authorized individual for the
25 particular purpose, meaning this class of therapy, he

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1 or she then has full authority under that
2 responsibility to make whatever modifications he or
3 she feels are appropriate to those techniques.

4 So if you give authorization to an
5 individual, you are essentially saying this person is
6 qualified to use this device in any manner in which he
7 or she feels is appropriate. Therefore, it behooves
8 us, as regulators or as advisors to regulators, to be
9 sure that those persons who are authorized in fact are
10 qualified to make those kinds of adjustments.

11 CHAIRMAN MALMUD: Thank you for that
12 clarification, Dr. Zelac.

13 I believe Dr. Nag wanted to say something.

14 MEMBER NAG: Well, I wanted -- if the
15 discussion is finished, I would like to make a motion
16 once the discussion is finished. But I would like
17 everyone to have the opportunity to have their
18 discussion heard.

19 CHAIRMAN MALMUD: Well, the discussion can
20 follow the motion.

21 MEMBER NAG: Okay. I would like to make
22 the motion that the -- for the NeoVista device, which
23 is under 35.1000, the training and experience
24 requirement would be under 35.400, to be someone in
25 the 35.400 or the user to be involved in the

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1 treatment. However, that person does not necessarily
2 have to be onsite or does not have to be physically
3 present during the treatment.

4 CHAIRMAN MALMUD: Is there a second to the
5 motion of Dr. Nag?

6 MEMBER THOMADSEN: Could you repeat the
7 motion?

8 CHAIRMAN MALMUD: Dr. Nag said that --

9 MEMBER THOMADSEN: I got lost somewhere.

10 CHAIRMAN MALMUD: -- a person should be an
11 authorized 35.400 user, to be involved in the therapy,
12 but that that individual need not be physically
13 present at the time of the therapy.

14 MEMBER NAG: And this can be modified to
15 make the language, you know, more appropriate. But
16 the idea is that the 35.400 -- I mean, the 35.400
17 person should be involved in the planning, and so
18 forth, in the protocol but does not necessarily have
19 to be present during the procedure. You know, we can
20 tighten up the language.

21 CHAIRMAN MALMUD: That is the motion on
22 the floor. Is there a second?

23 MEMBER THOMADSEN: I will second that.
24 This is Thomadsen.

25 CHAIRMAN MALMUD: Yes, Dr. Thomadsen.

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1 MEMBER THOMADSEN: I will second that.

2 CHAIRMAN MALMUD: The motion has been made
3 by Dr. Nag and seconded by Dr. Thomadsen. Now it is
4 open for discussion.

5 MEMBER EGGLI: This is Doug Eggli.

6 CHAIRMAN MALMUD: Yes, Dr. Eggli.

7 MEMBER EGGLI: I think sometimes perfect
8 is the enemy of good. If, as the retinal surgeons
9 tell us, if we make this too difficult, the procedure
10 will be abandoned and patients will not be offered
11 this procedure, I think we are doing a disservice to a
12 large, large number of patients with a disease leading
13 to blindness, which is a severe impairment in
14 lifestyle.

15 I think that I can support any
16 modification from the standard protocol requiring a
17 full court radiation oncology involvement. But in the
18 limited procedure, as described, which we hear from
19 the retinal surgeons is their intent, in spite of the
20 fact that the regulation allows you to do other than
21 that, I think that we really limit the availability of
22 a potentially useful therapy by making it too
23 difficult. Again, perfect can be the enemy of good.

24 MEMBER NAG: This is Dr. Nag. I would
25 like to ask Dr. Eggli, how will it limit, if the

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1 individual patient does not need to be seen by the
2 radiation oncologist, the radiation oncologist doesn't
3 have to be onsite, how would that limit? You can have
4 100 patients per month. The radiation oncologist,
5 they don't have wait for the radiation oncologist to
6 be -- to see them before they can be treated.

7 So I do not understand how it will limit
8 the access. Would you explain that to me, please?

9 MEMBER EGGLI: I will give you a
10 roundabout explanation. Again, we are talking about a
11 standard protocol, which has already been reviewed and
12 has had the input of the radiation oncology community
13 in its original design. And I see no added value to
14 adding a radiation oncologist on top of something that
15 is now a standard procedure, and dosimetry isn't going
16 to change it any. And even the process of having to
17 form a committee for this may cause some
18 ophthalmologists in practice to be dissuaded from even
19 pursuing it.

20 I think that if they follow the simple
21 standard practice, which has been evaluated by
22 radiation oncology and been deemed to be an
23 appropriate treatment algorithm, that the radiation --
24 if they follow the standard practice, the radiation
25 oncologist adds no additional value reviewing this

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1 once again.

2 MEMBER NAG: This is Dr. Nag again.

3 CHAIRMAN MALMUD: This is Dr. Malmud. Dr.
4 Eggli, are you suggesting that if the standard
5 protocol is followed, and not varied in any fashion,
6 that it would not require the continuing intervention
7 -- participation of a radiation oncologist?

8 MEMBER EGGLI: Yes. But that any
9 deviation from the protocol would.

10 MEMBER NAG: This is Dr. Nag. As Dr.
11 Zelac reminded us a few minutes ago, when this is
12 opened as a regulation, it is not protocol-dependent.
13 It is dependent on the class of applicators or the
14 class of radioactive material. And that point will
15 apply to the NeoVista device, irrespective of how it
16 is being used. That is point number one.

17 And that being the case, once this is put
18 in the regulation, if someone wants to change it, they
19 can. And that is a major problem.

20 Secondly, when you send that this protocol
21 has already had the input from the radiation
22 oncologist, why was that there? Because initially
23 when this was started, it required the input of the
24 radiation oncologist. If that requirement was not
25 there before, it would have started without any

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1 involvement, because obviously it takes a little
2 effort to try to get help from anyone else.

3 And unless you have that help from the
4 beginning, you are not going to --

5 MEMBER EGGLI: Well, the --

6 MEMBER NAG: So, again, having a radiation
7 oncologist will not delay anything.

8 MEMBER EGGLI: This is Eggli again. I
9 have to respectfully disagree with that. The protocol
10 was designed with the assistance of the radiation
11 oncology community, because that was an appropriate
12 input. And you're right, in the practice of medicine,
13 I can do almost anything I want. But I'm probably not
14 going to. I'm going to follow good practice.

15 And in the places where people are going
16 to vary from that, odds are they are going to do it on
17 protocol, and those protocols are involved -- will
18 involve a radiation oncologist to design those
19 clinical protocols. You know, you can't regulate
20 against the rare occurrence of something untoward, and
21 then deprive everybody of an opportunity for a very
22 beneficial treatment.

23 Essentially, I think that you are worried
24 about edge cases. And you can't -- you can never
25 regulate edge cases out of existence. I don't think

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1 that if the standard protocol is followed that the
2 continued involvement of the radiation oncologist adds
3 any value, and all of your arguments deal with the
4 retinal surgeon doing something different than the
5 standard protocol, which may or may not occur.

6 And my inclination is to listen to what
7 the retinal surgeon says, which is that they don't
8 anticipate that this deviation will occur. And if it
9 were, it would go back to the protocol stage. Do we
10 have any reason not to believe the input we are
11 getting from our professional colleagues in retinal
12 surgery?

13 CHAIRMAN MALMUD: Thank you both for your
14 comments. I would ask: are there any other members
15 of the committee who wish to make comments? I think
16 that the positions of Dr. Nag and Dr. Eggli are clear.

17 MEMBER GILLEY: Yes, this is Debbie.

18 CHAIRMAN MALMUD: I'm sorry. Who is this?

19 MEMBER GILLEY: Debbie Gilley.

20 CHAIRMAN MALMUD: Thank you, Debbie
21 Gilley.

22 MEMBER GILLEY: I have two, one to NRC
23 staff. I want to make sure that these guidelines do
24 not require adoption by the agreement states. Can I
25 get a confirmation on that, that they are just

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1 guidelines?

2 CHAIRMAN MALMUD: You are asking the
3 question of NRC staff.

4 MEMBER GILLEY: Yes, I am.

5 CHAIRMAN MALMUD: Anyone on the NRC staff
6 want to answer Debbie Gilley's question?

7 MS. FLANNERY: Yes, this is Cindy
8 Flannery. Debbie, the answer to your question is, no,
9 the agreement states are not required to adopt the
10 guidance. It is under 35.1000.

11 MEMBER GILLEY: Thank you. And the second
12 question I have, if you are going to have this team
13 approach, and we have a medical event, is the
14 radiation oncologist who now wants to be listed as
15 part of this team going to step up and be accountable
16 for activities that he had general overview for?

17 MEMBER NAG: Well, that would be part of
18 the requirement if you have an oversight. That person
19 would be playing an oversight role in the design and
20 overall responsibility. I mean, we have many other
21 instances where we have an overall responsibility of
22 radioactive material where they are, although we don't
23 necessarily see it every day. But we do oversight of
24 that, you know, in --

25 MEMBER GILLEY: You have missed my point.

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1 You have made it very difficult on the regulatory
2 community in implementing this to identify who should
3 be accountable in the event of a medical event. If
4 you remember when we did the cardiology that I -- the
5 intravascular brachytherapy, we didn't list the
6 cardiologist. We list the authorized user.

7 They were the ones that were responsible
8 as the medical person in the event of a medical event.

9 Now you were looking at putting two people as being
10 part of the team, and it concerns me in trying to
11 write regulations and implementation to have clear
12 guidance given to everyone as to what the
13 responsibilities are of both of these professions.

14 CHAIRMAN MALMUD: Debbie, I ask you a
15 question. Are you in support of the motion of Dr.
16 Nag, or opposing it?

17 MEMBER GILLEY: I am opposed to the
18 motion.

19 CHAIRMAN MALMUD: You are opposed to Dr.
20 Nag's motion.

21 MEMBER GILLEY: That is correct. I voted
22 when we met in October, and I stand by that vote.

23 CHAIRMAN MALMUD: Thank you for that
24 clarification.

25 DR. HEIER: I apologize. This is Jeff

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1 Heier. And I don't want to speak out of turn, but I
2 wonder if I could just make one point and ask one
3 question.

4 CHAIRMAN MALMUD: Please do.

5 DR. HEIER: The first point is, in any
6 clinical trial that we design, there is input of a
7 whole vast number of medical specialists. Every
8 clinical trial we looked at for AMD, we speak to a
9 cardiologist, we may speak to a pulmonologist, we may
10 speak to a neurologist, because treatments we are
11 going to do may have an impact in their area, and we
12 want their expertise in the design of the study.

13 Once we have had their expertise, they are
14 almost never further involved in the study. And that
15 is very common.

16 The question I have is, it is not clear to
17 me, if the proposal is to now have a radiation
18 oncologist as part of the team on every patient,
19 meaning they are going to have input into every
20 patient, because that, once again, will eliminate this
21 as a practical application for these patients. We see
22 them too often.

23 It is too hard to just coordinate with
24 their primary care physician or their families on the
25 extent of treatment. And if we are having to

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1 coordinate with another medical specialist, and it is
2 a fairly -- what you are proposing in terms of the
3 coordination is not simple now.

4 Now you are talking about changing
5 dosimetry and maximizing outcomes based on lesion
6 characteristics and lesion size. If these are things
7 that we agonize over and speak among our colleagues, I
8 can only imagine the type of intervention that is
9 going to occur if we have to do it with another
10 medical specialty. I think you eliminate it as a
11 practical approach.

12 CHAIRMAN MALMUD: Thank you. Thank you
13 for that information.

14 VICE CHAIRMAN VETTER: Dr. Malmud, this is
15 Dick Vetter. I just have a question for NRC. If we
16 approve this motion, how would they implement it?

17 CHAIRMAN MALMUD: Excuse me. Dr. Vetter?
18 Dr. Vetter?

19 VICE CHAIRMAN VETTER: Yes.

20 CHAIRMAN MALMUD: I am also going to ask
21 you to take it for another five minutes. I have
22 another patient to treat, and ask NRC to answer your
23 question.

24 VICE CHAIRMAN VETTER: Okay.

25 CHAIRMAN MALMUD: Thank you.

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1 DR. ZELAC: Dr. Malmud, this is Ron Zelac.
2 I think that the motion that Dr. Nag has put forth is
3 in fact consistent with respect to the requirements
4 for the authorized user for this device with our
5 current guidance. So, in effect, it would be an
6 endorsement of the current guidance and puts to the
7 side the motion that was made at the October meeting
8 concerning modified, substantially reduced training
9 and experience requirements for the authorized user
10 for this purpose.

11 So that is the answer to the question. If
12 you will indulge, I have something else I can add I
13 think.

14 VICE CHAIRMAN VETTER: Please do.

15 DR. ZELAC: It appears that there are
16 really two things going on here. One is concern to be
17 sure that patients who could benefit from this
18 treatment have an opportunity to receive it, meaning
19 specifically the protocol that is in place right now.
20 And the second is concern about the possibility that
21 authorized individuals could go on, using medical
22 judgment, and make modifications to the usage of this
23 device for select patients.

24 The suggestion I would have and throw out
25 for consideration is whether the Advisory Committee

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1 would be supportive of essentially letting your
2 previous recommendation stand with respect to the
3 training requirements, but limit those who are
4 authorized under those limited training requirements
5 to only be authorized to use this under the existing
6 protocol. That could be accomplished through a
7 license condition for anyone who was authorized for
8 491 use for this particular purpose.

9 In that way, you know, the persons who are
10 interested and wish to be participants in this
11 protocol could have access to the device for that
12 specific purpose, but yet not have the full range of
13 authority that would be associated with an open,
14 untethered authorization.

15 MEMBER NAG: This is Dr. Nag. Dr. Zelac,
16 I really liked your suggestion. And what I can do is
17 to reword my motion to basically say that for patients
18 being treated under the existing protocol, the 491
19 user would be sufficient. However, for the overall
20 use of the device under any other -- under any other
21 condition, it will require a 35.400 level user.

22 DR. HOWE: Dr. Nag, this is Dr. Howe. I
23 guess I have an underlying question. That is that we
24 know that there was a recent humanitarian
25 compassionate --

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1 MEMBER NAG: Exemption.

2 DR. HOWE: -- exemption, and we don't know
3 how that patient differed. Maybe the patient wasn't
4 qualified to be in the test. Maybe there was
5 something else. Now, you don't necessarily want to be
6 in a position where for the compassionate choices you
7 now have to go to a higher level. I mean, we are
8 already seeing some variation, and I don't know how to
9 address that. But I just want to bring it back to the
10 discussion.

11 MEMBER NAG: But, basically, I think what
12 we are trying to do is to make a fast track for the
13 large number of patients who will be treated by one
14 single means and have back on the fast track, so that
15 they could be seen by the ophthalmologist as an
16 authorized user. And any modification, therefore,
17 thereof, whether it is a humanitarian exemption,
18 whether it is someone trying a different dose,
19 etcetera, would have to be done under the supervision
20 of a 35.400.

21 I think this -- there would be only a
22 limited number of them, and I think it will provide a
23 good balance between excess and the overall safety.
24 And I think that is why I kind of support Dr. Zelac's
25 recommendation.

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1 MEMBER EGGLI: This is Eggli. I can
2 support this as well. And in response to Dr. Howe's
3 statement, even though it is compassionate use, it is
4 a different use that would benefit from the input of a
5 radiation oncologist, and probably should have it.
6 And, you know, compassionate use doesn't necessarily
7 always mean emergency use.

8 But I think that a formal dosimetry
9 planning would be very appropriate where you vary from
10 the protocol. So that -- I think that is perfectly
11 compatible with what we agreed to before. As long as
12 the practitioner agrees to practice the limited
13 protocol, then we can give a limited authorization.
14 If it is anything different, it requires a Part 400
15 authorization.

16 So that is perfectly compatible with what
17 I believe we agreed to in the last meeting.

18 MEMBER THOMADSEN: Dr. Vetter? This is --

19 VICE CHAIRMAN VETTER: There is -- I'm
20 sorry. If everyone could quiet down for a moment,
21 there is someone in the background trying to get our
22 attention, and the volume is very low. Go ahead,
23 please.

24 MEMBER THOMADSEN: Dr. Vetter?

25 VICE CHAIRMAN VETTER: Yes.

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1 MEMBER THOMADSEN: This is Bruce
2 Thomadsen.

3 VICE CHAIRMAN VETTER: Bruce.

4 MEMBER THOMADSEN: And the question for
5 the proposal is -- assume that the current trial will
6 close relatively soon, and a new trial will probably
7 open. Are we stating that we would be limiting people
8 to the -- limiting the retinal surgeons to what is in
9 the current trial, without regard to the next trial?
10 And if it turns out the next trial is doing better, do
11 we come back and revisit this each time there is a
12 trial and a change?

13 DR. HEIER: If I could -- I don't -- this
14 is Dr. Heier again. I don't know for certain that the
15 -- what the compassionate use was. But I know I
16 almost had a compassionate use, and the disease was
17 exactly the same. It was choroidal
18 neovascularization. But the patient didn't meet the
19 exact criteria of the study guidelines, which was a
20 visual acuity change.

21 And yet the disease -- the underlying
22 disease was exactly the same. And what I have seen in
23 compassionate use for diseases like this is the
24 compassionate use is usually for the same process --
25 choroidal neovascularization -- which by far the large

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1 majority are age-related macular degeneration. But
2 there are some other causes, like myopia and
3 histoplasmosis.

4 And those occasionally are what get the
5 compassionate use and not -- so it is the same
6 underlying problem, a growth of new blood vessels from
7 -- growing in a similar manner, but it is usually
8 patients who don't fit the exact criteria from the
9 study. It is not a change in the study application at
10 all. It is not a change in how it is delivered. It
11 is simply they didn't meet one of the criteria.

12 CHAIRMAN MALMUD: This is Malmud again.
13 Was that the question that you were asking, Dr.
14 Thomadsen?

15 MEMBER THOMADSEN: No, not at all. It was
16 -- I was not discussing the compassionate use, but
17 with the changes in a protocol, that a new protocol
18 would probably open once the old protocol changes.

19 CHAIRMAN MALMUD: Thank you. That's what
20 I thought you meant, Dr. Thomadsen. I think your
21 question might be best addressed to a member of the
22 NRC staff who was with us on this conversation. Would
23 a -- is this applicable only to the existing protocol?

24 DR. ZELAC: My thought personally, and
25 this is strictly only personally, would be that the

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1 license condition would limit the authorization of the
2 individual named to follow -- to be -- to use the
3 device in approved protocols, you know, FDA-approved
4 protocols for example.

5 CHAIRMAN MALMUD: Thank you, Dr. Zelac,
6 but --

7 DR. ZELAC: So if you went off of that,
8 then you'd be in another sphere entirely.

9 CHAIRMAN MALMUD: But you used the -- this
10 is Malmud again. Dr. Zelac, could you clarify this
11 for us? You used the plural "protocols." Does that
12 mean that it is beyond this single protocol?

13 DR. ZELAC: To me it does, because Dr.
14 Heier was speaking of this going from Phase 2 to
15 Phase 3, which I presume would be a different
16 protocol.

17 DR. HEIER: No.

18 DR. ZELAC: No? Same protocol?

19 DR. HEIER: It is in the pivotal phase
20 already.

21 CHAIRMAN MALMUD: Thank you, Dr. Zelac.

22 Dr. Thomadsen, Dr. Zelac says this is
23 applicable to protocols, with a plural.

24 MEMBER THOMADSEN: My question to Mr.
25 Zelac, then, is: when the protocol closes, does that

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1 mean that the practitioners would have no recourse to
2 treat their patients?

3 DR. ZELAC: My answer is yes, it would
4 have to come back to have the license condition
5 removed.

6 MEMBER THOMADSEN: So if I may clarify,
7 what we are saying is we are giving approval to
8 retinal surgeons to treat patients according to the
9 protocol on the protocol only. Is that their
10 authorization that we are approving?

11 CHAIRMAN MALMUD: This is Malmud. That is
12 my understanding of it. Dr. Zelac, is that your
13 understanding of it?

14 DR. ZELAC: Yes, it is.

15 CHAIRMAN MALMUD: Thank you. Now, with
16 that understanding, is there any change in concerns
17 regarding the approval?

18 MEMBER SULEIMAN: This is Orhan Suleiman.

19 CHAIRMAN MALMUD: Yes, Dr. Suleiman.

20 MEMBER SULEIMAN: Yes. Let me explain
21 something in terms of if the manufacturer decides that
22 they want to expand their indication or their -- or if
23 a user is trying to do experimentation of a
24 significant deviation, at some point it is not --
25 there is a questionable area, just like everything

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1 else, of when it is the practice of medicine and when
2 it is human research.

3 And so if it is practice of medicine to
4 treat a patient, and the changes that they are
5 advocating are within the overall scope of practice of
6 medicine, it is okay. But if they are really doing
7 experimentation and trying to test new protocols and
8 whatever, that is human research. It has got to come
9 under, you know, FDA umbrella, and the whole nine
10 yards again.

11 So I think the -- it is never an easy
12 answer. But I want to make clear that you've got
13 these different little areas that are actually
14 distinct, but they are not -- the borders are not
15 very, very sharp and clearly defined.

16 But there is following the protocol that
17 has already been approved in a very specific manner,
18 there is deviating from that under the practice of
19 medicine, which could be minor differences, you know,
20 which will have a significant, you know, change in
21 the patient safety and whatever, but how much you
22 start to deviate is a different issue.

23 If the physician is deviating in a very
24 terrible way, you know, then you get into litigation
25 and liability issues. If you are doing

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1 experimentation to come up with something very
2 different, very dramatic, and you are doing it in a
3 much more formal manner, then you are back into a
4 clinical trial environment. Those are very, very
5 different areas, and one size doesn't fit all, so I
6 think we -- I am just trying to remind the committee
7 members that we do have those differences.

8 So I think what Dr. Zelac is proposing
9 sounds like it has enough flexibility, but at the same
10 time assures enough safety -- radiation safety in
11 terms of patient protection.

12 CHAIRMAN MALMUD: This is Malmud again.
13 I'm going to -- as chair, I am just going to ask you
14 to clarify something, Orhan. Are you suggesting that
15 you are in favor of approval of this if it adheres to
16 the current protocol, and that it is limited to the
17 current protocol?

18 MEMBER SULEIMAN: Again, I am a little
19 confused in terms of how -- what are the radiation
20 safety or radiation dosimetry assurances. Does the
21 protocol in fact address that? Or what I'm hearing
22 also is that, if it is under practice of medicine, is
23 it possible you may deviate enough that you may change
24 the dosimetry characteristics, that you may cause a
25 safety issue?

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1 CHAIRMAN MALMUD: For the dosimetry issue,
2 may we refer either to a radiation oncologist or to a
3 radiation physicist?

4 MEMBER SULEIMAN: Well, somebody who knows
5 what they are doing.

6 CHAIRMAN MALMUD: That is why I chose
7 those.

8 MEMBER SULEIMAN: Yes.

9 MEMBER THOMADSEN: Well, certainly,
10 depending what the changes you want to make are, if it
11 is the criteria for accepting a patient, no. If it is
12 going to be sizes of lesions, yes. So, I mean, that
13 depends.

14 MEMBER NAG: Again, I think that is where
15 -- the way I had framed my motion was that, if it is
16 exactly opposing the current protocol, then that is
17 fine. But anything that is already in the dose,
18 whether it be notifying the patient, and so forth, or
19 number of areas that are irradiated, then it does
20 require a 400 user to be involved.

21 MEMBER THOMADSEN: And the patient has --

22 CHAIRMAN MALMUD: I'm sorry. Who is
23 speaking now?

24 MEMBER THOMADSEN: I'm sorry. This is
25 Thomadsen again.

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1 CHAIRMAN MALMUD: Thank you.

2 MEMBER THOMADSEN: And in some of the
3 patient selection criteria, such as diabetes, for
4 example, it would definitely affect how the patient
5 responds to radiation. So there are -- while some
6 things would change the dosimetry, some things would
7 change the effects of the dosimetry.

8 DR. HEIER: This is Jeff Heier again. I
9 certainly agree with that, and those are there for a
10 reason. But there are certain things that are there
11 just because it is a study. And, for instance, any
12 AMD study that treats wet macular degeneration has
13 visual acuity guidelines. And usually it is vision of
14 20/40 or worse.

15 Yet when the treatment is approved, those
16 are automatically wiped out. Every single AMD study
17 that has had approval in the last 10 years has had
18 those same criteria. And once the drug is approved,
19 then the visual acuity criteria is wiped out. And
20 those are usually there solely so you can demonstrate
21 certain degrees of improvement.

22 If a patient starts with 20/20 vision,
23 they are not going to be able to gain three lines of
24 vision. So they keep those patients out of the study
25 intentionally.

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1 MEMBER THOMADSEN: And is the proposal
2 that if once -- let's say this meets approval, the
3 study is successful, and there are those guidelines.
4 Is the proposal that when patients meet those
5 guidelines, that disease with that criteria, you can
6 treat them in a medical setting? It is not that the
7 patient has to be in a study protocol to be treated.

8 VICE CHAIRMAN VETTER: Yes. This is Dick
9 Vetter. My understanding of this is that what we are
10 approving are the training and experience requirements
11 for medical use, for routine clinical use once this
12 protocol is completed. Is that correct? Maybe Cindy
13 Flannery can clarify that.

14 MEMBER THOMADSEN: Can Dr. Zelac address
15 that? Because that was my question before, and the
16 answer was it was just for this protocol.

17 DR. HEIER: Right. Which makes no sense
18 to train people, have them do it all, and then say,
19 "Okay. You've done it, you've been successful, now we
20 have to retrain you differently."

21 DR. ZELAC: This is Zelac. I understood
22 from Dr. Heier and the discussion at the last meeting
23 that we are talking about a specific -- in terms of
24 inclusion for the patient, a specific limited size
25 lesion, one treatment with a particular given

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1 angulation of the device, and that's it. Correct?

2 DR. HEIER: Correct. That is correct.

3 DR. ZELAC: Now, my intent was essentially
4 to, in appropriate fashion with wording, limit the
5 authorizations of individuals as authorized users to
6 that, to that particular use, and not to offer -- open
7 it up to variations in any one of those
8 characteristics, be it, for example, dose painting as
9 being within the realm of the authorization.

10 MEMBER NAG: This is Dr. Nag. This is
11 what I was afraid of, that we will be going to a
12 slippery slope. Once we allow a limited application,
13 then the next thing will be, well, we have this
14 limited application. This is somewhat similar, so
15 that point will extend to that. And, you know, you
16 change a few other things, very much similar, so,
17 therefore, it doesn't require any further approval,
18 and so on.

19 So, you know, that leads to a slippery
20 slope. And, therefore, I had only -- in my motion I
21 had only said in this particular protocol, and then,
22 if there is some other new protocol coming in, we can
23 reexamine that, see whether that makes sense, before
24 we give approval for that protocol.

25 CHAIRMAN MALMUD: So the -- my

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1 understanding -- this is Malmud. My understanding is
2 that we are approving a use-specific approval. Is
3 that correct, Dr. Zelac and Dr. Nag?

4 MEMBER NAG: Well, that was my intention,
5 that this -- that the 491 user, authorized user, would
6 be for this particular protocol. And if anything else
7 changes, it goes under the 400 user until, you know,
8 they bring back anything else on the table and we
9 examine it and see whether that would be something
10 that can go back to a 491 user.

11 CHAIRMAN MALMUD: Thank you. Dr. Zelac,
12 was that your understanding also?

13 MS. FLANNERY: He just stepped out. This
14 is Cindy Flannery.

15 CHAIRMAN MALMUD: Cindy, is that your
16 understanding?

17 MS. FLANNERY: Well, I just want to
18 clarify that when the recommendation was made at the
19 October meeting, it was not clear or specific to --
20 you know, when the recommendation was made for 491 to
21 be adequate for the T&E, it didn't really specify
22 whether it would be just for the clinical trial
23 protocol or for any use.

24 MEMBER EGGLI: This is Eggli. If you look
25 at statements of consideration, I think in the

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1 discussion, again, the intent of the motion was that
2 it was for this protocol as applied to clinical
3 patients, once the FDA approves this protocol. So
4 what we are talking about is not per se a research
5 protocol, but a clinical treatment protocol. It was
6 the intent of my motion to limit the authorization to
7 that treatment protocol.

8 MS. FLANNERY: And I not sure that
9 everybody understood it that way. And the reason why
10 I say that is because one person on ACMUI, you know,
11 abstained, and with the reason being that when this
12 device gets approved it could be used off label. And,
13 you know, the T&E that was being suggested in the
14 motion might not be adequate, and it was too early to
15 tell. So I -- I'm not certain that everybody in the
16 ACMUI understood it that way.

17 CHAIRMAN MALMUD: Thank you. Dr. Vetter,
18 you chaired that session of ACMUI. Do you recall what
19 the feeling was? I know what the minutes said, but do
20 you recall what the spirit of the committee was?

21 VICE CHAIRMAN VETTER: This is Dick
22 Vetter. I can only say what my understanding was, and
23 it was exactly as Dr. Eggli outlined. It was limited
24 to once the clinical trial was complete, and the
25 procedure is approved by FDA, that it would be limited

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1 to this 24 Gray standard procedure.

2 CHAIRMAN MALMUD: Thank you. Thank you
3 for clarifying that again.

4 So that was the spirit and the decision of
5 the committee in the October meeting on day 2. And
6 now, the motion on the floor -- before us today, Dr.
7 Nag's motion, reaffirms that. Is that correct, Dr.
8 Nag?

9 MEMBER NAG: Yes. Except that I added
10 that for any other uses it has to be under 35.400. So
11 I basically clarified the previous one, because the
12 previous was slightly ambiguous because it didn't
13 state, you know, what happens if it is not on that
14 particular protocol.

15 CHAIRMAN MALMUD: But in a brief
16 statement, your motion simply says that if there are
17 any changes it has got to go under 35.400. Is that
18 it?

19 MEMBER NAG: Yes. That if it is done
20 under the current protocol, 35.491 authorized user is
21 sufficient. However, if there are any deviations or
22 alterations, it has -- there has to be a 35.400
23 authorized user involved.

24 CHAIRMAN MALMUD: And that is your motion
25 with us today.

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1 MEMBER NAG: Yes.

2 CHAIRMAN MALMUD: May we move the motion,
3 it being five after three? Or does anyone else have
4 something they wish to say?

5 MEMBER LIETO: This is Ralph Lieto. I --
6 just for clarification, to be sure I understand, when
7 you say "involved," you mean that he would be -- that
8 they would have to have an AU on the license --

9 MEMBER NAG: Yes.

10 MEMBER LIETO: -- for this use. That's
11 what you mean by "involved," correct?

12 MEMBER NAG: So what I had said in my
13 previous one was that a 35.400 authorized user would
14 have to be involved, but does not have to be
15 physically present during the procedure.

16 CHAIRMAN MALMUD: So by "involved," do you
17 mean it has to have an authorized user who does not
18 need to be physically present?

19 MEMBER NAG: Yes.

20 CHAIRMAN MALMUD: Thank you. May we move
21 the motion?

22 MEMBER MATTMULLER: This is Mattmuller,
23 Dr. Malmud.

24 CHAIRMAN MALMUD: Yes.

25 MEMBER MATTMULLER: First of all, I want

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1 to come out and say that I am in full support of Dr.
2 Eggli's position on a number of the points he made.
3 My concern with Dr. Nag's amendment is that, does this
4 -- with the way it is worded, would this preclude, if
5 yet another protocol was verified through a clinical
6 trial, that the individual couldn't use this device
7 under 491, it would have to then go to 490?

8 MEMBER NAG: Well, basically, my intention
9 is that this protocol has been approved. We have
10 noted that, and, therefore, it is approved for this
11 protocol. If there is a new protocol that is made, it
12 is very easy to bring it back and say, "This is a new
13 protocol. Is this acceptable?" And if we find it
14 equally acceptable, we'll say yes. If we find that,
15 you know, that new protocol is for some reason not
16 acceptable or not safe, we do have the right to say
17 that.

18 CHAIRMAN MALMUD: Does that answer your
19 question, Dr. Mattmuller?

20 MEMBER MATTMULLER: Yes, it does. Thank
21 you.

22 CHAIRMAN MALMUD: Thank you. Call the
23 motion? All in favor, aye?

24 MEMBER THOMADSEN: Excuse me. Can you
25 please read the motion back, so we are quite clear on

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1 exactly what we are voting on?

2 CHAIRMAN MALMUD: Thank you. Who was
3 speaking?

4 MEMBER THOMADSEN: That is Thomadsen
5 again. Sorry.

6 CHAIRMAN MALMUD: Thank you, Dr.
7 Thomadsen. Dr. --

8 MEMBER NAG: Nag?

9 CHAIRMAN MALMUD: -- Nag?

10 MEMBER NAG: Okay. I make the motion that
11 for this NeoVista device, under the present protocol,
12 a 35.491 use -- authorized user will be acceptable.
13 If there are any deviations or changes from the
14 protocol, it will require the involvement of a 35.400
15 authorized user who does not necessarily have to be
16 present during the procedure.

17 CHAIRMAN MALMUD: Thank you. Does that
18 clarify your question, Dr. Thomadsen?

19 MEMBER THOMADSEN: Yes. Thank you.

20 CHAIRMAN MALMUD: Thank you. If we may,
21 we will call the question. All in favor of Dr. Nag's
22 notion?

23 (Chorus of ayes.)

24 All opposed to Dr. Nag's motion?

25 (No response.)

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1 All --

2 MEMBER GILLEY: Aye.

3 CHAIRMAN MALMUD: So there is one
4 opposition.

5 MEMBER GILLEY: Yes.

6 CHAIRMAN MALMUD: Is that you, Debbie?

7 MEMBER GILLEY: Yes, that's me.

8 CHAIRMAN MALMUD: Thank you.

9 MEMBER GILLEY: Thank you.

10 CHAIRMAN MALMUD: Any abstentions?

11 (No response.)

12 So the motion moves forward with all in
13 favor except for one.

14 MEMBER NAG: How many ayes were there?

15 CHAIRMAN MALMUD: How many ayes were
16 there? Shall we -- let's count the ayes. Please
17 identify yourselves by your vote.

18 MEMBER NAG: Dr. Nag, yes.

19 CHAIRMAN MALMUD: Nag, yes.

20 VICE CHAIRMAN VETTER: Vetter, yes.

21 CHAIRMAN MALMUD: Vetter, yes. Lieto?

22 MEMBER LIETO: Yes.

23 CHAIRMAN MALMUD: Yes.

24 MEMBER SULEIMAN: Suleiman, yes.

25 CHAIRMAN MALMUD: Mattmuller?

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1 MEMBER MATTMULLER: Yes.

2 MEMBER EGGLI: Eggli, yes.

3 CHAIRMAN MALMUD: Thank you.

4 MEMBER THOMADSEN: Thomadsen, yes.

5 MEMBER FISHER: Fisher, yes.

6 CHAIRMAN MALMUD: Thank you. Other
7 members of the committee? Malmud is a yes, if you
8 want my vote.

9 MEMBER NAG: Thank you.

10 CHAIRMAN MALMUD: Thank you. Does that
11 answer your question, Dr. Nag?

12 MEMBER NAG: Yes.

13 CHAIRMAN MALMUD: And does that meet the
14 requirements of an approval?

15 MS. FLANNERY: Yes, it does. This is
16 Cindy Flannery.

17 CHAIRMAN MALMUD: Thank you, Cindy.

18 That I believe covers the items on the
19 agenda for today. Are there any other informational
20 items or comments from the public that we would
21 entertain?

22 (No response.)

23 If not, I want to thank all of the
24 participants, both the members of the committee, the
25 NRC staff, and the public, for their participation,

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1 and wish you all a very happy holiday season and a
2 healthy new year. And we look forward to our next
3 committee meeting.

4 Thank you.

5 (Whereupon, at 3:10 p.m., the proceedings in the
6 foregoing matter were adjourned.)

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