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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

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6 MEETING

7 + + + + +

8 OPEN SESSION

9 + + + + +

10 MONDAY,

11 APRIL 28, 2008

12 + + + + +

13 The Committee met at 8:00 a.m. in Room T2-
14 B3 at Two White Flint North, 11545 Rockville Pike,
15 Rockville, Maryland, Leon S. Malmud, Chairman,
16 presiding.

17 COMMITTEE MEMBERS:

18 LEON S. MALMUD, M.D., Chairman

19 RICHARD J. VETTER, Ph.D., Vice Chairman

20 DOUGLAS F. EGGLE, M.D., Member

21 DARRELL R. FISHER, Ph.D., Member

22 DEBBIE B. GILLEY, Acting Member

23 RALPH P. LIETO, Member

24 STEVE MATTMULLER, Member

25 SUBIR NAG, M.D., Member

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1 COMMITTEE MEMBERS: (cont.)

2 SALLY W. SCHWARZ, Member

3 ORHAN H. SULEIMAN, Ph.D., Member

4 BRUCE R. THOMADSEN, Ph.D., Member

5 WILLIAM A. VAN DECKER, M.D., Member

6 JAMES S. WELSH, M.D., Member

7

8 NRC STAFF PRESENT:

9 STEPHANIE BUSH-GODDARD, RES

10 CINDY FLANNERY, FSME

11 SANDY GABRIEL, Region I

12 DONNA-BETH HOWE, Ph.D., FSME

13 TONY HUFFERT, RES

14 PENNY LANZISERA, Region I

15 ROB LEWIS, FSME

16 ANGELA R. McINTOSH, FSME

17 CHARLIE MILLER, FSME

18 ASHLEY TULL, FSME

19 MARTY VIRGILIO, OEDO

20 DUANE WHITE, FSME

21 RON ZELAC, Ph.D., FSME

22

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ALSO PRESENT:

LYNNE FAIROBENT, AAPM

EDNA GARCIA-PENA, Walter Reed

EMILY GARDNER, ASNC

MIKE PETERS, ACR

DOUG PFEIFFER, AAPM

AMANDA POTTER, APPM

SERGIO SANTIVIAGO, ACC

HARRY SKENE, Geisinger

GARY STAPOLKEY, Walter Reed

CINDY TOMLINSON, SNM

ANN WARBICK CERONE, MDS Nordion

NANCY WERSTO, FDA

EMILY WILSON, ASTRO

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2
3 P-R-O-C-E-E-D-I-N-G-S

4 8:14 a.m.

5 CHAIRMAN MALMUD: Ladies and gentlemen, if
6 we may, we will begin this morning's open session of
7 the Advisory Committee on the Medical Uses of
8 Isotopes, The opening statements will be made by
9 Cindy Flannery and by Robert Lewis of the NRC.

10 Cindy, would you formally open the meeting
11 for us. Thank you.

12 MS. FLANNERY: Thank you. As a Designated
13 Federal Officer for this meeting I am pleased to
14 welcome you to Rockville for the public meeting of the
15 ACMUI. My name is Cindy Flannery. I am the team
16 leader for the Medical Radiation Safety Team within
17 the Medical Safety and Events Assessment Branch.

18 The federal officer is required for this
19 Advisory Committee in accordance with 10 CFR Part
20 7.11. In the absence of a designated federal officer
21 as the alternate DFO I will serve as the federal
22 officer for this meeting and until such time as the
23 vacancy is filled.

24 This is an announced meeting of the
25 Committee. It is being held in accordance with the

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1 rules and regulations of the Federal Advisory
2 Committee Act and the Nuclear Regulatory Commission.

3
4 The meeting was announced in the March 18,
5 2008 edition of the Federal Register. The function of
6 the Committee is to advise the staff on issues and
7 questions that arise on the medical use of byproduct
8 material. The Committee provides counsel to the staff
9 but does not determine or direct the actual decisions
10 of the staff or the Commission. The NRC solicits the
11 views of the Committee and values their opinions.

12 I request that whenever possible we try to
13 reach a consensus on the various issues that we will
14 discuss today but I also recognize there may be a
15 minority or dissenting opinions. If you have such
16 opinions, please allow them to be read into the
17 record.

18 As part of the preparation for this
19 meeting I have reviewed the agenda for member and
20 employment interest based upon the very general nature
21 of the discussion that we are going to have today. I
22 have not identified any items that would pose a
23 conflict of interest for the members. Therefore, I
24 see no need for an individual member of the Committee
25 to recuse themselves from the Committee's decision-

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1 making activities.

2 However, if during the course of our
3 business you determine that you have a conflict
4 relative to the matters before the committee please
5 state it for the record and recuse yourself from that
6 particular aspect of the discussion.

7 At this point I would like to introduce
8 the individuals seated at the table today. Dr. Leon
9 Malmud, Healthcare Administrator, ACMUI Chair; Dr.
10 Richard Vetter, Radiation Safety Officer, ACMUI Vice
11 Chair; Mr. Steve Mattmuller, our incoming Nuclear
12 Pharmacist; Ms. Sally Schwarz, outgoing Nuclear
13 Pharmacist; Mr. Ralph Lieto, Nuclear Medicine
14 Physicist; Dr. Subir Nag, Radiation Oncologist; Dr.
15 William Van Decker, Nuclear Cardiologist;

16 Dr. James Welsh, Radiation Oncologist; Dr.
17 Darrell Fisher, Patient Advocate; Dr. Bruce Thomadsen,
18 Therapy Medical Physicist; Ms. Debbie Gilley, the
19 Acting State Government Representative. Ms. Gilley
20 will listen and speak on behalf of the Agreement
21 States and is serving in an acting capacity until her
22 NRC employment paperwork has been processed.

23 Dr. Orhan Suleiman, FDA representative and
24 Dr. Douglas Eggli, Nuclear Medicine Physician will not
25 be attending the morning session of this meeting.

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1 They will be joining us later on today.

2 Dr. Malmud, ACMUI Chairperson, will
3 conduct today's meeting. Following a discussion of
4 each agenda item Dr. Malmud at his option may
5 entertain comments or questions from members of the
6 public who are participating with us today.

7 At this time I will now turn the meeting
8 over to Mr. Robert Lewis, Division Director for
9 Material Safety and State Agreements.

10 MR. LEWIS: Good morning, ladies and
11 gentlemen. It is also my pleasure to welcome you to
12 Rockville for this meeting of the Advisory Committee
13 on the Medical Uses of Isotopes. This is my first
14 meeting of ACMUI since I took the position of Director
15 of the Division of Material Safety and State
16 Agreements this February. It's very nice to meet you
17 all, and I'm looking forward to working with you.

18 Also, I have the great pleasure to
19 formally welcome Mr. Steven Mattmuller, the new
20 Nuclear Pharmacist Representative. Let me take this
21 opportunity to thank all of you for taking on this
22 important role. We really wish you success during
23 this turbulent period in the materials regulatory
24 program. We really are looking forward to the advice
25 you can give us on the regulatory initiatives underway

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1 in security and in safety.

2 In the past year the agency has embarked
3 upon a comprehensive program to improve our licensing
4 process in the changing security environment. We have
5 issued increased controls and fingerprinting orders to
6 all the licensees that have larger sources to control
7 access to the material.

8 We have also been responsive to Government
9 Accountability sting operation where they successfully
10 obtained an NRC license under fraudulent purposes. We
11 have also very proactively considered recommendations
12 of the National Academy of Sciences on alternatives
13 and replacement to radioactive sources which we will
14 hear about later this morning as well. Finally, we
15 expanded our authority to include accelerator produced
16 radioactive materials in the last year. That, of
17 course, has a large bearing upon the medical industry.

18 In the coming year we are going to develop a
19 national source tracking system and a web-based
20 licensing system that will really reinvent our
21 regulatory approach and interface with our licensees.

22 The period of increasing expectations on NRC on
23 Agreement States and on licensees regarding material
24 security will continue in the coming year and may
25 easily even amplify.

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1 Finally, we have in the international
2 arena development of new basic safety standards and
3 recommendations by ICRP and NCRP that will have
4 bearing upon our fundamental radiation protection
5 approaches as regulators in America.

6 We are going to need your assistance to
7 provide insights on the impacts of all of these
8 initiatives on the medical uses of radioactive
9 material for diagnosis and therapy. I encourage you
10 to critically examine and question my actions or the
11 NRC staff's actions. If we don't have those
12 questions, we won't arrive at the best answer
13 together.

14 I offer a standing personal invitation to
15 help explain any projects that we have underway upon
16 which you may have questions or to clarify any
17 expectations or opportunities for the ACMUI to
18 participate early and often as these programs develop
19 and mature.

20 On the lighter side, although today is an
21 exception, this is probably the best time of year in
22 Washington, D.C. area. I hope you have some time
23 during your work and spare moments to get out and
24 enjoy the weather and the flowers.

25 At this point I would like to hand the

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1 meeting over to the Chair, Dr. Malmud.

2 Dr. Malmud, I know you were going to
3 introduce Charlie Miller for some comments but he is
4 held up at an operations meeting upstairs so he'll be
5 here any moment but he's not ready yet.

6 CHAIRMAN MALMUD: Shall we wait for
7 Charlie or shall we move on with the next item on the
8 agenda?

9 MR. LEWIS: I think we can move on.

10 CHAIRMAN MALMUD: Move on?

11 MR. LEWIS: Yes, that would be wise.

12 CHAIRMAN MALMUD: In that case, the next
13 item on the agenda would be a discussion of PET
14 radiopharmaceutical production. Sally Schwarz has
15 that item on the agenda.

16 The other announcement I would like to
17 make early in the meeting is that when any of you
18 speaks, would you please introduce yourself so that
19 the court stenographer can capture your name before
20 your statement. Thank you.

21 MS. SCHWARZ: As you know, my name is
22 Sally Schwarz. What I'm going to be speaking to you
23 today about in a timely manner is the clinical
24 production of PET Radiopharmaceuticals and essentially
25 the problems that we encounter in running these

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1 operations.

2 I just wanted to mention briefly a little
3 historical overview of PET. In the 1970s the PET
4 scanner itself was initially developed by Dr. Michel
5 Ter-Pogossian at Washington University. Then
6 throughout the '80s, and I actually arrived at
7 Washington University in 1976, at that time they were
8 already performing clinical studies involving O-15
9 labeled water. They were actively involved in
10 performing research.

11 In the '80s they developed what is known
12 as Baby Cyclotrons. Currently at Washington
13 University we have two of the older cyclotrons that
14 actually accelerate protons and deuterons and we have
15 a new Baby Cyclotron that accelerates negative ions.
16 The advantage to this development of the Baby
17 Cyclotron is that the negative ion acceleration causes
18 less activation of the machine itself so it is
19 actually easier to shield this machine and have it
20 available in a facility.

21 Our older machines are actually positioned
22 in the basement, actually below the basement, so they
23 have a sub-basement area that has been developed to
24 place these machines so that they are away from our
25 working personnel.

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1 Also in the '80s instrumentation,
2 hardware, software for the PET imaging process
3 improved significantly. Overall in the beginning
4 these PET facilities did develop at academic
5 institutions that were using the machines for research
6 opportunities.

7 In the '90s PET itself developed into a
8 clinically useful tool. Initially Syncor and
9 Mallinckrodt were two companies that began to
10 distribute F-18 labeled FDG as unit doses to an area
11 outside surrounding them essentially. It's an
12 expensive operation to have a cyclotron, the personnel
13 to operate the cyclotron and do the synthesis, quality
14 control, and deliver product.

15 The universities this was available
16 because they had the cyclotrons but the regular
17 community in smaller hospitals that didn't have
18 cyclotrons couldn't afford to invest in the technology
19 so the ability just to purchase unit doses of these
20 regulated compounds was provided by corporations,
21 Syncor and Mallinckrodt at the time, in the '90s.
22 Then the biggest push that moved us to clinical
23 utility was that Medicare began to reimburse, pay for
24 PET studies and that occurred in June of 1998.

25 The workhorse of PET is F-18 fluoride.

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1 Half-life is roughly 110 minutes so if you can imagine
2 what we are asked to do is to produce an isotope,
3 synthesize compounds, perform quality control, and
4 deliver products to our patients. Again, this is a
5 very difficult operation in the sense of the half-life
6 of the radionuclides.

7 The mode of decay is 100 percent positron
8 emission and the maximum energy of the positron for F-
9 18 is .64 MeV. The common method currently used to
10 produce F-18 is a PN reaction, radiation of enriched
11 O-18 water with protons, a neutron out of the nucleus
12 to make the F-18 radionuclide.

13 This is just a photograph of RDS 111
14 machine essentially. This is an example of the Baby
15 Cyclotron. This one is produced by CTI Siemens
16 Corporation. Actually, as you can see on one of these
17 -- does this project if I -- what you are seeing here
18 essentially is the machine. It has an external shield
19 that doesn't move as well as the machine itself is
20 shielded by a moveable shield. You can see the tracks
21 towards the bottom there where the shields slide out
22 to expose the actual cyclotron itself.

23 Back up one. What we are seeing here this
24 is the stationary shields. These are the movable
25 shields and the tracks that allow us to expose the

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1 actual cyclotron.

2 DR. NAG: About what size, I mean, a human
3 being?

4 MS. SCHWARZ: They are about five and a
5 half to six feet tall. They are not large compared to
6 the older machines that were kind of massive machines.

7 The diameter is about, I want to say, eight feet in
8 diameter. Again, this is an example when they were
9 installing our machine.

10 The actual shields are open. This is the
11 cyclotron. It operates under a vacuum. We never open
12 it typically unless we are working on this machine.
13 This is just the machine itself that actually is
14 pulled apart to expose the ion source. This is the
15 location of the gas that we ionize to produce the
16 negative ion that we accelerate. These are the Dees.

17 There are four Dees and the charge on
18 these Dees actually changes 10 to the 6 time per
19 second. What we are trying to do essentially is
20 attract this negative ion to the positively charged
21 Dee and this requires obvious synchronization to
22 manage to keep the machine in tune such that they are
23 accelerating this correctly.

24 CHAIRMAN MALMUD: Sally.

25 MS. SCHWARZ: Yes.

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1 CHAIRMAN MALMUD: May I take this moment
2 to interrupt you. I'm sorry. We have an important
3 issue to address and Dr. Miller is here to address it.

4 Just remain where you are for the moment and I'll
5 introduce Dr. Miller. Charlie Miller.

6 DR. MILLER: Thank you, Dr. Malmud. I
7 apologize for interrupting the presentation. This is
8 a special occasion because it's Sally's last meeting
9 with the Committee and I wanted to personally thank
10 her for all of her wonderful service to the Committee
11 over the years. If you will indulge me for just a
12 minute, I would just like to highlight some of her
13 most significant accomplishments.

14 She has been a nuclear pharmacist on the
15 Committee since 2000. In that light I think that she
16 has really provided some great counsel, especially as
17 it relates to the pharmacy aspects of what we do. It
18 really allowed a voice to be heard on this committee
19 with regard to the pharmacist perspective on things
20 that we have to be concerned about.

21 Also, she aided in the transition for
22 regulating NARM by reviewing and commenting on the
23 NARM rulemaking and guidance documents from her
24 perspective. I think that is extremely important.
25 She served on numerous subcommittees over time. As

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1 everyone knows that sits on the Committee, your
2 schedules are extremely busy so subcommittee
3 participation I know is highly appreciated by myself
4 and the staff.

5 For example, Part 35 T&E. She shaped the
6 alternate pathway for authorized nuclear pharmacists.

7 New Modality Subcommittee she served on and the Dose
8 Evaluation Subcommittee. Without further ado, what I
9 would like to do is present you with this certificate
10 to thank you for all your wonderful service to the
11 Committee. We are sorry to lose you.

12 MS. SCHWARZ: Thank you very much. I have
13 enjoyed the time that I have served on this Committee.

14 It has been a true learning experience. I mean, it
15 has opened my eyes to a number of issues, overall
16 regulatory direction, and I really feel that certainly
17 you have broadened my horizons.

18 I am hoping, as mentioned, that I have
19 offered something in return to the Committee. It has
20 been a very worthwhile experience to be able to serve
21 on this Committee. It has been enjoyable to meet all
22 of the individuals who are on the Committee as well.
23 Thank you.

24 CHAIRMAN MALMUD: Thank you, Dr. Miller.
25 Thank you, Sally. Sally, the entire Committee seconds

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1 Dr. Miller's comments. We very much appreciate all
2 the efforts that you have put forth on the Committee,
3 your talent, and we will miss you.

4 MS. SCHWARZ: Thank you very much. I
5 appreciate that.

6 CHAIRMAN MALMUD: Now, having interrupted
7 you, you can resume your presentation.

8 MS. SCHWARZ: This is kind of how my life
9 goes. As you noticed from the call this morning, my
10 cyclotron is not working and the first thing they do
11 is notify me which makes me think I am in the right
12 position at the right time. I shall continue.

13 This is, again, the ion source. What we
14 do is we use hydrogen gas and there is an electrical
15 field. The gas is ionized and essentially then there
16 is a split opening in this source. Actually it is
17 placed when the machine is paused in the center here.

18 Again, these ions are pulled into the machine due to
19 the current.

20 This is just an example of we have
21 produced the F-18 fluoride. Then we have to move it
22 from the cyclotron, from the vault where it's located.

23 Again, just as an aside, the actual exposure of the
24 machine, these newer machines for running dual
25 targets, 60 MeV beam currents. If we open the door

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1 and walk into our vault, right inside the vault we are
2 probably talking five or six mR per hour so compared
3 to the old machines you couldn't go in the vault where
4 you are operating a positively charged particle
5 machine.

6 Then, again, if the machine is turned off
7 it is essentially not radioactive as you turn it off.

8 I mean, it might be one to five mR per hour but,
9 again, relatively easy to work in this area. Then the
10 isotope has actually brought shielded conduits under
11 the floor up to the synthesis modules. Again, these
12 are lead shielded modules -- excuse me, hot cells
13 where we contain our modular system

14 This is an empty cell on the right-hand
15 side. We have connections for gas lines, electrical
16 lines. Then what happens is we close the door, bring
17 the fluoride into the synthesis module and we actually
18 run lines that run from the module up to our product
19 port.

20 The product port is connected to a sterile
21 pyrogen-free vial that is located in the lead shield.

22 This is then what we do only having to open this
23 ante-room door rather than the actual hot cell to
24 access the final product again reducing exposure to
25 the personnel who are working in the area.

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1 Here we notice that we have shielded
2 exhaust filters. We have carbon filters that traps
3 in-line so that if we have fluoride exhausted out the
4 hot cell before it's essentially traveling to the
5 exterior exhaust we trap it. It's shielded again so
6 it can decay in-house before it is essentially
7 distributed out of the facility.

8 DR. VETTER: During a synthesis if someone
9 were to open that door, what would the exposure rate
10 be?

11 MS. SCHWARZ: We don't do that.

12 DR. VETTER: Just say very high.

13 MS. SCHWARZ: It is very high. I mean, we
14 are working -- it depends, of course, on our starting
15 material of our synthesis nodule. We start production
16 for FDG in our facility, and we are now distributing
17 with 4 curie F-18 fluoride so if it would be in the
18 middle of that synthesis, it would be extremely high.

19 Actually, one of our SOPs is that under no
20 circumstances are we to open those hot cell doors.

21 We have a clinical population waiting for
22 this product so there is always that urgency felt that
23 we need to deliver product but I have always stated I
24 take the responsibility if the product fails. We have
25 a centralized pharmacy that we can call to, again,

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1 possibly back us up if we do have problems but we
2 don't open the cells.

3 This is just an example of the FDG module.

4 This one happens to be made originally by coincidence
5 of Belgium metal which now has been taken over by GE.

6 It's a wonderful module. As you can see, it's kind
7 of color-coded reagents which are batch produced like
8 a pharmaceutical batch of product for each of the
9 reagents used in this synthesis.

10 We have a chemist that comes in when we
11 begin our cyclotron operation at 4:00 in the morning.

12 We run until about 6:00. We have a chemist that
13 comes in to set up these modules at 5:30, 5:15.
14 Again, what they are doing is putting all of the lines
15 in place, the reagents in place. Then once we are
16 ready, we close the hot cell door and the fluoride is
17 then brought from the cyclotron under pressure,
18 delivered directly to the box so there is no handling
19 of the radioactive materials.

20 This is the schematic that we see on our
21 computer screen and follow the process. I also wanted
22 to note on the last screen these are TV monitors
23 essentially and where we focus them they are not
24 scanning the entire contents of the hot cell but we
25 focus them on the critical spots so we can actually

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1 observe. If we have problems that we might
2 anticipate, at least we know what is going on. Again,
3 we don't open this cell but it gives us a heads up as
4 to what is going on.

5 We then can follow the process. We
6 actually have radiation monitors in place along the
7 line of the synthesis so as each of the reagents is
8 being added we can see the activity being moved from
9 position to position. Again, this is the final
10 product vial but, as I mentioned, it is located in the
11 ante-port so that we watch the delivery but it's
12 actually going into a shielded sterile vial in the
13 antechamber.

14 So we finally finish the product. It's
15 taken us two hours for the cyclotron, half an hour to
16 run this process, and now we have to perform quality
17 control because we have patients waiting. Typically
18 we deliver about 22 to 25 doses a day for these
19 patient studies. We just installed a second CT PET
20 scanner and potentially at this point we are looking
21 to a third to double our patient number.

22 Then quality control. This has to be done
23 for every batch that we produce and it has to be done
24 before we release the product for injection for human
25 use. Again, as you can see, the list is extensive and

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1 it is significant quality control.

2 First of all, we check the radionuclidic
3 identity to assure that we have made the right
4 isotope. We check the pH and that also is a clear and
5 colorless solution that we have made and, again, using
6 ALARA technique. We are not lifting the vial out of
7 the shield. We are examining a sample, and this is
8 acceptable by FDA.

9 We perform the radiochemical purity. We
10 use TLC for the quality control. You may remember
11 this from your chemistry somewhere in the past where
12 you are separating out different colors on those
13 little TLC strips. Again, we use this to separate out
14 the impurities in the solutions that we make.

15 We also check for residual solvents. We
16 have FDA limits that are being incorporated into our
17 United States pharmacopeia as we speak. We also test
18 for any potential chemicals that would be there. We
19 use Kryptofix in this reaction which is actually a
20 toxic chemical. The limits are set by the FDA, and we
21 have to assure that our product is less than 50
22 micrograms per mil for Kryptofix.

23 We also have to check the filter. These
24 solutions that we make, again, we are preparing final
25 sterile products on a batch-per-batch for human use.

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1 Sterility testing requires two weeks so there is no
2 way we can complete sterility testing before we
3 release this product. What we do is we assure that
4 the filters that we use that are the final
5 sterilization method for our product have an intact
6 filter.

7 We remove the filter from the synthesis
8 module. We actually apply pressure to this filter and
9 make sure that it is intact. If it is, we can assume
10 that our product is sterile. We still do sterility
11 testing. Within 24 hours of preparing each of these
12 products they are inoculated immediately and we wait
13 for two full weeks to assure that they were sterile
14 when they were injected.

15 If there is a problem with the final
16 product testing, we then have to go back and
17 revalidate our process if we find it's not a sterile
18 product. I will tell you that in all the years I've
19 been doing this we have not had non-sterile products.

20 We have had operator errors. We have had to
21 reinoculate our products to retest the final product.

22 Our actual products have been sterile so processes
23 are well-defined in terms of what we are preparing for
24 humans.

25 Also the bacterial endotoxin test is

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1 performed before release and that does give us a
2 definite idea. Bacterial endotoxin is a product of
3 bacteria, yeast, and mold so if we had bacteria
4 present, we would have endotoxin present. If we are
5 negative on that test, we are assured pretty
6 substantially that the products are fine for human
7 injection.

8 These are just examples of the instruments
9 that we use to perform a quality control. This is the
10 TLC scanner. That is the quality control for
11 radiochemical purity. The output is assayed. This is
12 a gas flow detector. We essentially scan that TLC
13 plate and we get this chromatogram.

14 What this shows is essentially we have a
15 single peak that actually is defining FDG. If we had
16 an impurity it would run typically at the origin of
17 our plate, or there is another impurity that
18 potentially could be present so we have documented the
19 known impurities and we are looking for the final
20 product quality. Again, the person on your left is
21 performing gas-chromatograph injection. This is
22 looking for the residual solvents that we possibly
23 could have from this reaction.

24 I wanted to go through briefly the uptake
25 of FDG into the cell is really essentially a

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1 nonspecific uptake. It's taken into the cell
2 similarly to glucose. I know that Dr. Welsh will be
3 speaking later in the morning or later in these days
4 about another agent for PET imaging because there's
5 many more specific types of agents being developed but
6 FDG is our work horse currently and the way it is
7 taken up is because all cells utilize glucose.

8 Tumor cells typically have an up-
9 regulation of the amount of glucose that they take
10 into the cell so they can concentrate it over normal
11 tissues. The thing that they can't do FDG when it's
12 in the cell has this fluoride attached to the glucose
13 structure which doesn't allow full metabolism of this
14 compound. Glucose is metabolized to a state of carbon
15 dioxide and water but FDG is actually trapped in the
16 cell once it's brought into the cell so that is the
17 basis. It's just the entrapment for us to be able to
18 localize it externally.

19 When we image patients we actually have to
20 assure because we are looking at glucose levels that
21 they have not eaten. We are trying to keep them in a
22 fasted condition at least four to six hours before
23 injection. We measure their glucose levels in the
24 blood.

25 Again, this image on your left is a normal

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1 uptake image so what you're seeing is up-taking the
2 normal liver, up-taking your kidneys that are then
3 excreting FDG through the ureters into the bladder.
4 That is a normal biodistribution study for FDG.
5 Again, the patient is in the scanner with their arms
6 over their head which you can see here and there is
7 uptake in the facial area.

8 That would be normal. This is an example
9 of a CT PET image looking at the fused image of the
10 metabolic image, looking at the uptake in the primary
11 breast cancer. In the CT scan you can see there is,
12 again, uptake noted in the CT. This gives you the
13 anatomical location and metabolic location and the
14 image is being fused to allow the exact location to be
15 determined for the various types of tumors or
16 metastatic disease.

17 It doesn't work for all types of tumors
18 but it certainly does work for a significant number of
19 tumors. Again, an example of lung cancer, primarily
20 lung cancer in this case You can see, again, the
21 anatomic image and the fused image.

22 So once we've prepared this product in our
23 facility we then have to deliver it and this is
24 usually accomplished in our facility either of two
25 ways. We are a 20-minute walk from our clinical area

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1 and we do that just using manual Biodex transport
2 boxes that allow us to transport a certain amount of
3 activity.

4 We do use the DOT transport labels even
5 though we are traveling within our university license.

6 We are not going exterior. Later in the day our
7 radiation safety truck actually picks up the bulk of
8 our product and delivers it by regular DOT transport.

9 The next isotope I want to talk a little
10 bit about is certainly not routinely used in every
11 institution of the United States but there is an
12 ongoing clinical trial using O-15 labeled water and
13 oxygen that is located about 25 sites throughout the
14 United States. The primary investigator was at
15 Washington University and he has recently moved to
16 North Carolina but he is involved with the carotid
17 occlusion surgical study.

18 I wanted to give you a little oversight
19 because it is a pharmaceutical that is certainly used
20 routinely. Half-life has two minutes so, again, even
21 more complicated than 110-minute half-life. 100
22 percent positron emission and maximum beta energy 1.74
23 so significantly higher than with fluoride.

24 Common methods of production. Depending
25 on the type of machine that you have you can use

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1 either deuterons or protons. Now, the Baby Cyclotrons
2 can product either deuterons or protons. The GE can
3 produce either. The CTR machine accelerates only
4 negative ions, the hydrogen ion and, therefore, only
5 proton availability.

6 You can use either naturally occurring
7 nitrogen irradiation with deuterons to make the O-15
8 or enriched nitrogen irradiation with protons to make
9 O-15. This, of course, when you are dealing with
10 enriched target materials to produce an isotope it's
11 always more expensive so we prefer if possible to do
12 this N-14 irradiation.

13 In our institution we actually have both
14 possibilities and our primary machine right now is
15 still our older machine for making O-15. Once we make
16 the oxygen we can actually deliver it directly to the
17 patient as the oxygen gas or we can formulate it into
18 carbon monoxide gas or into O-15 labeled water using
19 another module. It's not platinum, it's palladium
20 catalyst over 420 degrees.

21 For this oxygen delivery, again I want you
22 just to understand these short-lived materials and
23 delivering them for use in our sites. We actually
24 deliver our O-15 2,000 feet from our cyclotron
25 facility. Essentially two blocks we deliver this O-15

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1 labeled gas. There are actually gas lines which run
2 in conduit at the exterior of our pneumatic line tube
3 transfer system.

4 I'll show you that pretty soon but the
5 conduit is actually maintained under vacuum and it's a
6 loop that actually exhausts back to our cyclotron
7 vault. Again, it's going up to the facility. We
8 actually use it to prepare our water and if it is for
9 some reason a problem and it's not utilized, it is
10 sucked back into our cyclotron vault for safety
11 purposes.

12 These transfer lines are remote from
13 public space, and we do maintain acceptable exposure
14 rates at 30 centimeters from the gas lines. We do
15 measure them as well. All of our lines are labeled
16 with radioactive material stickers and they are
17 regulatory inspected.

18 This is the CTI Siemens O-15 water module
19 and this, again, sits right next to -- we have three
20 of these modules that sit right next to our PET
21 scanners so we deliver the oxygen up to the PET suite
22 and we onsite prepare these radiopharmaceuticals.
23 Again, what's happening is hydrogen gas is combining
24 -- this is non-radioactive hydrogen combined with
25 oxygen. The O-15 we deliver from the 2,000 feet and

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1 it's over palladium catalyts. We do produce water on
2 site.

3 This is just an example. You can see the
4 millipore filter that I mentioned before. It is the
5 same kind of millipore filter. From this synthesis
6 module that is actually shielded it is then delivered
7 through this millipore filter into our product
8 syringe. This whole setup is setup in a laminar flow
9 space so that, again, it's acceptable for producing
10 the final product according to the FDA.

11 This then is not normally sitting on top
12 of our dose calibrator. It is actually in behind a
13 lead shield but this is just so I could photograph the
14 setup of this operation.

15 Again, quality control. Same thing. We
16 have to do all the same type of quality control
17 testing before we can release this material. What the
18 FDA has allowed us to do is to, actually the USP, is
19 to define a quality control batch. During the day we
20 just do QC on the very first batch because obviously
21 if we are going to take 20 minutes to do quality
22 control on a two-minute radionuclide, we have nothing
23 left for our patients. What we do is do a quality
24 control on the first batch and then release the final
25 product.

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1 Just an example of what we are using this
2 for. This is a cost study, the carotid occlusion
3 surgical study. We are actually utilizing water and
4 oxygen to identify a subgroup of patients with
5 symptomatic carotid artery occlusion. This particular
6 group of patients are at high risk for subsequent
7 ipsilateral ischemic stroke on current medical
8 therapy. We are trying to determine whether they are
9 good candidates for surgery.

10 Again, we are going to use these
11 pharmaceuticals to identify a risk factor for stroke.

12 We are going to look for the amount of increased
13 oxygen extraction fraction in the brain. Again, this
14 is a noninvasive technique and something that cannot
15 be performed without the use of these radioactive
16 materials.

17 We will also identify a treatment that
18 will reduce the risk factor and this is actually
19 external carotid to internal carotid bypass surgery.
20 Then we want to determine if this treatment actually
21 reduces stroke risk.

22 These are images that are obtained. The
23 first is to look at the cerebral blood flow in the
24 brain. The second one is to look at the amount of
25 oxygen that your brain is actually extracting and then

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1 essentially this is a combined imagine process
2 mathematical but it is, again, looking at the amount
3 of metabolism ongoing.

4 We need to maintain the brain's metabolism
5 at a certain rate. If you don't have enough blood
6 flow essentially, you need to extract more oxygen from
7 the blood that is there in order to maintain your
8 metabolism.

9 How do you know all this is ongoing? We
10 are going to use these radioactive materials. This
11 particular top patient here has good collateral
12 circulation because this person looking at his oxygen
13 extraction fraction is a normal image. Here you see
14 good profusion, good extraction and, again, normal
15 metabolism. This person obviously having had a
16 stroke, having problems with these carotid arteries,
17 has developed on his own good collateral circulation
18 to accommodate increase in blood flow.

19 This particular patient has poor
20 collateral. This is reduced blood flow and this is
21 increased oxygen extraction fraction. Once we see
22 this increase in oxygen extraction fraction we know
23 the brain is working too hard and the blood flow to
24 the brain is not sufficient. If we look at a patient
25 that was selected for this bypass surgery, essentially

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1 this is the preoperative image and this is essentially
2 reduced blood flow if you look at normal being up in
3 the yellow region and this green is essentially
4 reduced.

5 Again, with the oxygen extraction fraction
6 this significant is at about 50 percent and normally
7 you would like it closer to the blue range. After the
8 surgery, the bypass surgery again, we are seeing blood
9 flow return more to normal. Again, the extract
10 fraction is returning to normal.

11 The next isotope, and last actually, I
12 want to talk about is C-11 and this, again, is an
13 isotope that is used for a lot of research ongoing
14 currently. A number of things including Alzheimer's
15 types of compounds at our institution.

16 This 20-minute half-life, again, is a
17 challenge. Not quite as difficult as the two-minute
18 half-life. Again, positron decay by 100 percent and,
19 again, an intermediate energy for the positron for the
20 O-15. Common method of reduction is to use N-14
21 bombarded with protons to make C-11.

22 This is just quickly a Grignard reaction.
23 Again, if you took organic chemistry you at least
24 heard the word Grignard before. It is probably long
25 in your past and not too interesting. What we do with

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1 this particular production is to use carbon dioxide.
2 That is what is made in the cyclotron. We then mix it
3 with methyl magnesium bromide to make this
4 intermediate.

5 Essentially at that point this
6 intermediate is actually heated to remove ether
7 because ether is a solvent and we don't want to
8 inject too much ether in our patients. Then we add
9 acid to cleave the magnesium bromide and to give us
10 the final C-11 labeled acetate product. Again, this
11 is purified by distillation into normal saline and
12 then sterile filtered to that blue millipore filter
13 that I mentioned previously.

14 This is just a schematic of the Siemens
15 CTR module. Again, the carbon dioxide is being
16 brought up from the cyclotron and delivered to a
17 reaction vessel that is shielded that you can't see.
18 Again, the reaction occurs and we are going to then
19 heat back, drive off the ether, and then we are going
20 to distill it. After we add the acid we distill it
21 into that normal saline vial.

22 This is not shielded you can notice
23 sitting up here in the air. Again, this is in a hot
24 cell and, again, the exposure to the personnel working
25 with these hot cells is very acceptable. My chemist's

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1 hand doses typically can run anywhere from about 200
2 millirem in a month to 1,300 to 2,000 millirem in a
3 month depending on what they are doing. Routine
4 production personnel are really down in about 300
5 millirem a month. Again, we develop process. That
6 takes more hand dose and then once it's automated and
7 moved into the routine production hand doses drop.

8 Again, all the same kinds of quality
9 control but this time not like the 0-15 labeled QC
10 batch we actually perform the quality control on the
11 final product that will be injected in the person.
12 This is probably our maximal challenge. We then
13 prepare acetate and typically we deliver it by one of
14 two means, either a 20-minute walk to the other
15 facility, that's a half-life. Again, we are talking
16 about having to start with several curies to deliver a
17 20 millicurie dose or 30 millicurie dose to a patient
18 often times.

19 Again, this is just an example of one of
20 my chemists who is actually drawing a dose. You can
21 see he is wearing sleeves, safety glasses, and gloves,
22 using tungsten syringe shields to remove his doses.
23 This is actually the FDG or the C-11 acetate final
24 product vial. We move it from the hot dell into this
25 particular rotational device so we can draw these with

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1 limited dose to our personnel.

2 This is delivery of our C-11 acetate.
3 Once it's been drawn into a syringe we remove the
4 needle. We put on a sterile cap and then we place it
5 into what looks like an automated bank transfer
6 system. This is actually PEVCO Systems which is a
7 commercial unit. We put this drawn dose into another
8 tungsten syringe shield which is then loaded into our
9 transport sender and delivered 2,000 feet to our PET
10 facility.

11 Overall just as far as uptake, we use this
12 C-11 acetate to look for prostate carcinoma. The
13 reason for that is typically we also utilize it in our
14 cardiac studies for a number of different studies but
15 the one I will show you today overall for the
16 myocardium it would normally be shunted into the TCA
17 cycle.

18 For our tumor cell they actually
19 incorporate acetate preferentially into lipids. Since
20 acetate is preferentially metabolized to the lipids in
21 the tumor cells because cell growth proliferation
22 necessitates membrane constituents. This is, again,
23 hypothesis and not defined but it was determined by
24 Yoshimoto in 2001.

25 This is just a comparison. As I

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1 mentioned, FDG is our work horse but it's really not
2 good for everything. This is just a comparative of C-
3 11 acetate FDG. FDG, remember, normal distribution to
4 the liver and to your kidneys. You will see ureters
5 and bladder.

6 Again, C-11 acetate normal by distribution
7 is to the liver and the pancreas. As you can see, the
8 whole abdominal area is relatively clear of normal
9 activity. Typically if we are looking for prostate
10 carcinoma, we are looking for primary and metastatic
11 disease in the abdomen.

12 This is just an example of prostate
13 carcinoma. What we are seeing with the FDG, again,
14 we've got this ureter activity and bladder from normal
15 FDG as compared to the ability for the acetate to look
16 at the uptake in the nodes that are abnormal. Again,
17 this uptake is pancreas which is normal for acetate.

18 Again, normal biodistribution compared to
19 possibly the uptake that would occur with a tumor. We
20 need to essentially look at various pharmaceuticals
21 because certainly they are not all equal in terms of
22 their ability.

23 Does anyone have any questions for me?

24 CHAIRMAN MALMUD: Thank you, Ms. Schwarz,
25 for a magnificent overview of the production of PET

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1 pharmaceuticals from scratch to the finished product
2 and applications both FDA approved and still under
3 research. The Fluorine-18 products are FDA approved
4 and the oxygen products not yet.

5 MS. SCHWARZ: That's correct.

6 CHAIRMAN MALMUD: But you are at the place
7 that is a forefront so we appreciate being brought up
8 to date, or more up to date probably than most people.

9 I'm sure there are some questions for you.

10 Dr. Vetter.

11 DR. VETTER: Just real quickly. On the C-
12 14 acetate for prostate metastases is it detecting a
13 lymph flow or is it actually labeling to cancer cells?

14 MS. SCHWARZ: It's probably in lymph
15 nodes. Into the lymph nodes.

16 DR. VETTER: So it doesn't necessarily
17 indicate metastatic cancer. It simply indicates that
18 it could be occurring. I'm a little puzzled there.

19 MS. SCHWARZ: I think it was determined if
20 that was metastatic disease.

21 DR. VETTER: Okay. So it is laid in the
22 cancer cells.

23 MS. SCHWARZ: Yes, yes, yes.

24 CHAIRMAN MALMUD: Dr. Nag.

25 DR. NAG: These are very short-lived

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1 isotopes. The F-18 I know has been done in almost
2 every place. If you don't have cyclotron at your own
3 site how do you do F-18? Second, if you don't have a
4 cyclotron at your center, can you use another one?

5 MS. SCHWARZ: Well, FDG -- excuse me, any
6 foreign-labeled compound is readily available
7 depending on who your institution may be we are able
8 to work with. I know that PETNET and Cardinal Health
9 certainly have cyclotron operations and deliver as far
10 as FDG to a significant. I doubt that there is any
11 place that they couldn't deliver FDG to.

12 They are in the process of developing new
13 F-18 label tracers because for them it is essentially
14 impossible to deliver C-11 labeled unless some
15 organizations actually have onsite PETNET operations
16 and, in that case, yes, they could be making carbon-11
17 labeled compounds for them. As far as delivering
18 carbon-11 or oxygen-15 it would be impossible.

19 DR. NAG: With half-life unless you have a
20 cyclotron within the same city how do they do it?

21 MS. SCHWARZ: What do you mean? How do
22 they produce it and get it delivered to your site?

23 DR. NAG: Yes.

24 MS. SCHWARZ: What they do is they start
25 very early in the morning. Typically their day starts

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1 at 11 p.m. and they run their cyclotrons and produce
2 significant quantities. They are probably per run 8
3 to 10 curies of starting fluoride activity and they
4 will deliver depending on what time you ask for your
5 calibration they will have to draw up, say, 400
6 millicuries to be able to deliver you a dose at the
7 appropriate time because it will leave their facility
8 to be air shipped or shipped by normal car transport
9 but they send a lot more out the door than what you --

10 DR. VETTER: They actually fly it all
11 around the country. You run it to the airport, put it
12 on a plane that is waiting, fly it to wherever it
13 goes, somebody is waiting to pick it up.

14 DR. NAG: Basically the transport has to
15 be worked out that within about three to four hours
16 it's from the plant and to the hospital within about
17 four or five hours.

18 MS. SCHWARZ: Exactly. They do that.
19 They really do have contracts with air carriers. Each
20 of these companies distributes their materials through
21 transport.

22 CHAIRMAN MALMUD: Dr. Welsh.

23 DR. WELSH: Is C-11 acetate likely to get
24 approved anytime in the near future? Do you have a
25 prediction on that for clinical use?

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1 MS. SCHWARZ: We do use it clinically.
2 The thing that we are working under is essentially
3 listed in the United States Pharmacopeia. There is a
4 monograph if you are able to produce the drug.
5 Essentially I worked with our clinicians so that they
6 are the ones ordering the compounded
7 radiopharmaceutical. That is able to be accomplished
8 at this time.

9 DR. WELSH: I think I meant Medicare
10 reimbursement.

11 MS. SCHWARZ: Oh. Well, that we still
12 will be a bit longer to accomplish that.

13 CHAIRMAN MALMUD: Malmud. I just wanted
14 to clarify something for Dr. Nag and that is that the
15 fluorine-18 radiopharmaceuticals are currently
16 available throughout the United States. The oxygen
17 and carbon are not yet approved and are available only
18 in the research facilities that are producing them.

19 I have a question for Ms. Schwarz. Are
20 you currently producing those for any other
21 institutions in St. Louis or just at Wash U.?

22 MS. SCHWARZ: Oxygen-15?

23 CHAIRMAN MALMUD: Yes.

24 MS. SCHWARZ: Just for Washington
25 University. We can't travel them far enough.

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1 Actually, PETNET is involved with that O-15 clinical
2 trial so they are onsite at certain academic centers
3 that are undertaking the use of this material under an
4 investigational new drug application. Bill Powers is
5 the holder of the IND now at North Carolina and all
6 the sites are fitted under this IND.

7 CHAIRMAN MALMUD: Thank you.

8 Yes, another question.

9 MS. GILLEY: Debbie Gilley. What is the
10 possibility of having mobile cyclotron for production
11 of these short-lived isotopes at locations? What is
12 the feasibility of that?

13 MS. SCHWARZ: They do have mobile
14 scanners. You know that. I would say it would be an
15 expensive operation to try to have. I mean, I could
16 see -- I mean, I'm thinking of weight. Even the small
17 cyclotrons to move them around would be -- I know they
18 were originally were talking desktop cyclotrons but
19 that never really evolved.

20 CHAIRMAN MALMUD: Yes, Dr. Fisher.

21 DR. FISHER: AccSys has developed a low
22 rate proton accelerator for producing F-18 in a mobile
23 system.

24 MS. SCHWARZ: How effective is it?

25 DR. FISHER: It works. I don't think any

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1 mobile systems have yet been sold in the U.S.

2 MS. SCHWARZ: The reason I ask about the
3 accelerator, is it a linear accelerator?

4 DR. FISHER: It's a linear accelerator.

5 MS. SCHWARZ: We tested that at Washington
6 University. We were part of the Department of Energy
7 team that worked on an accelerator. We were able to
8 produce O-15. There were plans. And we did work on F-
9 18, but it was not very successful. This is a number
10 of years ago so I do know that technology has
11 certainly been evaluated.

12 DR. FISHER: It's evolving technology.

13 MS. SCHWARZ: Right.

14 CHAIRMAN MALMUD: Any other questions?

15 DR. VAN DECKER: Yes, Van Decker. Just
16 for my interest sake, what percentage of your C-11
17 work in either acetate or palmitate is actually being
18 used towards myocardium metabolism?

19 MS. SCHWARZ: About 90 percent. We
20 actually do have a cardiologist on our staff who is
21 very actively involved in cardiac research and he does
22 studies that are essentially called gap studies, C-11
23 labeled acetate, palmitate, and glucose. We make a C-
24 11 labeled glucose as well.

25 What he is doing is looking at how the

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1 cardia metabolism is altered with various types of
2 disease state. He is a significant user of our C-11
3 compounds. Probably for our prostate imaging we may
4 do on the average of one a week. Sometimes we are
5 doing two but typically I would say on average one.

6 CHAIRMAN MALMUD: Any other questions for
7 Dr. Schwarz? If not, thank you again.

8 MS. SCHWARZ: You're welcome.

9 CHAIRMAN MALMUD: Congratulations again.

10 MS. SCHWARZ: Thank you very much.

11 CHAIRMAN MALMUD: The next item on the
12 agenda is Ashley Tull. The next person on the agenda,
13 excuse me, is Ashley Tull you will present the item
14 which is old business.

15 MS. TULL: Good morning.

16 CHAIRMAN MALMUD: Good morning.

17 MS. TULL: There is a new handout coming
18 out. I think there are some handwritten changes on
19 the copies you received. I have some lovely color
20 copies for you that are updated with new handwritten
21 notes.

22 Basically I'm going over all of the old
23 recommendations from all of 2007. We had a June
24 meeting, August, September, and October, and December.
25 We have 51 items to cover. This is just to give you

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1 a status of what we are working on, where things are,
2 how we are moving along. If anyone has any comments,
3 feel free to jump in. I'm just going to go through
4 each one one by one.

5 For the first one I'm going to read each
6 recommendation. NRC staff should issue an (IN), which
7 describes errors previously made and provides examples
8 of best practices with regards units of AKS vs.
9 apparent activity (mCi) for brachytherapy sources.
10 The IN should be done in collaboration with the
11 American Association of Physicists in Medicine and
12 coordinated with Agreement States.

13 Cindy has written this. I believe
14 everyone has received a copy of the draft and provided
15 comments so now we are incorporating ACMUI comments
16 and it's going through office concurrence. Anything
17 more on that?

18 Moving along. No. 2, NRC staff should
19 remove the attestation requirement for board certified
20 individuals and rewrite the attestation requirement
21 for individuals seeking authorization under the
22 alternate pathway. The rewritten attestation should
23 not include the word "competency" but should instead
24 read "has met the training and experience
25 requirements."

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1 You guys are going to talk to the
2 Commission tomorrow about this specific item so we
3 will leave that as pending and just leave it at that.

4 For No. 3, NRC staff should revise the
5 regulations so that board certified individuals, who
6 were certified prior to the effective date of
7 recognition or were certified by previously recognized
8 boards listed in Subpart J of the previous editions of
9 Part 35, are grandfathered.

10 This is in regard to the AAPM or the
11 Ritenour petition. This is pending and is
12 predecisional as well so I think everyone knows where
13 that one is.

14 For No. 4, NRC staff should reduce the
15 200-hour radiation safety training requirement to 120
16 hours for individuals seeking authorization under the
17 alternate pathway in 10 CFR 35.390. This was not
18 accepted. We received a management decision on this.

19 This is something that was decided in 2005 between
20 the Agreement States, ACMUI, and NRC staff. 200 was a
21 compromise so it is going to remain at 200. Any
22 comments? Okay.

23 No. 5, NRC staff should not change the
24 current definition of RSO. This recommendation was
25 accepted, and we are not pursuing rulemaking.

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1 No. 6, NRC staff should add the words "or
2 equivalent" so it is clear that information included
3 in a letter is the same as that which would have been
4 submitted in NRC Form 313A. This is accepted and will
5 be included in a UserNeed memo for consideration for
6 future rulemaking.

7 DR. NAG: Can you clarify "or equivalent"
8 is for what kind of things?

9 MS. TULL: This is a letter that can
10 basically instead of filling out form 313A saying yes,
11 they have met all the T&E requirements, you can just
12 put that in a letter format and someone can sign it.
13 Does that answer your question, Dr. Nag? Okay.

14 Ralph.

15 MR. LIETO: Why can't they just go into
16 the guidance document? I guess I'm trying to
17 understand why does it need to be delayed when you
18 could put that right into the guidance right off the
19 bat or on the website where the form is at.

20 MS. TULL: I don't think we can put
21 anything in guidance.

22 MS. FLANNERY: No, I think the regulations
23 need to change. This is really getting into the
24 burden, so it allows -- instead of just requiring
25 somebody to fill out a form 313A it would also allow

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1 them to write a letter. The way that the regulations
2 are written I believe would maybe make the burden
3 different.

4 DR. NAG: I think we just need to clarify.
5 313A is training and education requirement.

6 MS. FLANNERY: That's right.

7 DR. NAG: I think maybe that's not clear
8 to everybody.

9 MS. TULL: Any other questions on that
10 one? Okay, No. 7. NRC staff should revise 10 CFR
11 35.50(c)(2) to include AUs, AMPs, or ANPs identified
12 on any license or permit that authorizes similar types
13 of use of byproduct material. Additionally, the AU,
14 AMP, or ANP must have experience with the radiation
15 safety aspects of similar types of use of byproduct
16 material for which the individual is seeking RSO
17 authorization. This recommendation was accepted and
18 will be put in a User Need Memo for consideration for
19 future rulemaking.

20 No. 8, NRC staff should remove the
21 attestation requirement from 10 CFR 35.50(d) for AUs,
22 AMPs, and ANPs seeking RSO status, if the AU, AMP, or
23 ANP seeking RSO status will have responsibilities for
24 similar types of uses for which the individual is
25 authorized. Same thing on this. This was accepted

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1 and will be put in a User Need memo for consideration
2 for future rulemaking.

3 The next rulemaking should start later
4 this year as the current rulemaking that is on 35.40
5 and 35.3045 which is Written Directives and Medical
6 Event reporting. We are currently working on that.
7 As that begins to come to a close we'll start a new
8 rulemaking. These items would be considered in that
9 rulemaking to give you a better idea.

10 For No. 9, ACMUI tabled the following
11 issue until the next full ACMUI meeting. These were
12 proposed Part 35 changes that Donna-Beth had given so
13 you will see recommendations on these for the next
14 meeting.

15 NRC staff should allow more than one RSO
16 on a license with a designation of one RSO as the
17 individual in charge. NRC should create a Regulatory
18 Issue Summary to inform the regulated community of
19 NRC's interpretation. The RIS should be sent to ACMUI
20 and the Agreement States for review and comment.

21 We did go to our Office of General Counsel
22 on this, and they said it was not permitted under the
23 current regulations. You would need to pursue
24 rulemaking on this if there was to be a change. We
25 will still issue a RIS, though, to state our

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1 interpretation that it is not allowed under current
2 regulations. Any comments on this?

3 CHAIRMAN MALMUD: Mr. Lieto.

4 MR. LIETO: When was this decision made?

5 MS. TULL: The interpretation from Office
6 of General Counsel was made a few months ago.

7 MS. FLANNERY: Since the last meeting it
8 was brought up.

9 MS. TULL: We sent them a memo and said,
10 "Can you please tell us whether or not this would be
11 allowed?" They wrote back and said "No" which just
12 means it's not allowed under the current rule and we
13 would need to pursue a rulemaking.

14 DR. NAG: Does that mean that only one RSO
15 need a license?

16 MS. TULL: Yes.

17 CHAIRMAN MALMUD: A question arising from
18 this. What would be required in order to introduce
19 new rulemaking so that there could be more than one
20 RSO?

21 MS. TULL: Recommendation from ACMUI would
22 be a start. Then it would go to a User Need memo. If
23 NRC staff accepted the recommendation it would be
24 considered by the rulemaking staff when it's in the
25 User Need memo.

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1 CHAIRMAN MALMUD: Should there be a
2 discussion item on our agenda for this meeting
3 regarding that? I ask that question because as
4 Chairman I was aware of the unanimity of the Committee
5 with respect to the need for this change. Therefore,
6 since the entire Committee seemed to be interested in
7 this change for very practical reasons, it seems to me
8 we should fast track it to the degree allowable under
9 the rules.

10 That would be to make a motion at this
11 meeting regarding that change. That would be to make
12 a motion at this meeting regarding a recommendation
13 for a rule change. My question, therefore, is this
14 the moment to do it or shall we do this later in the
15 agenda?

16 DR. NAG: I think now.

17 MS. TULL: There is no specific agenda
18 topic for this.

19 CHAIRMAN MALMUD: Would a member of the
20 Committee, other than the Chair, wish to make that
21 motion?

22 DR. THOMADSEN: So moved.

23 MR. LIETO: Second.

24 CHAIRMAN MALMUD: Dr. Thomadsen makes the
25 motion and Mr. Lieto seconds the motion. The motion

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1 is that the NRC should revisit the rules regarding
2 allowing more than one RSO on a license identifying
3 clearly that if there is more than one RSO on a
4 license that there would be an RSO who has the
5 ultimate responsibility in that situation. By
6 allowing a second RSO it would create a more efficient
7 system for RSOs to relocate if they wish to. Is that
8 the motion?

9 DR. THOMADSEN: That's the motion.

10 CHAIRMAN MALMUD: Dr. Thomadsen says that
11 is the motion. Any discussion of the motion? Mr.
12 Lieto.

13 MR. LIETO: I guess, you know, since this
14 really originated from a presentation that I made, I
15 guess I'm a little distressed that the Committee was
16 pretty much unanimous about supporting that a decision
17 is made, it's not accepted, and we don't even hear
18 about it.

19 MS. TULL: It was sent in an e-mail
20 January 10th. This was the updated chart that I sent
21 out to everyone and I believe that one said it. If
22 not, I sent another one in early April that definitely
23 included this. The answer is not "No there can't be."
24 It's "No, it's not permitted under the current
25 regulations." Therefore, we need to proceed for a

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1 different pathway. NRC is not saying, "No, we are
2 going to reject this if you make the current motion
3 that is on the table."

4 MR. LIETO: What I'm asking for is how
5 that decision was made. When I researched this there
6 was nothing that NRC staff found anywhere in policy or
7 regulatory space that precluded it and that was the
8 information that came back to me both at a regional
9 and at a headquarters level.

10 All of a sudden it changed and yet none of
11 that information that went into this decision was
12 communicated. I guess that is what I'm asking for.
13 Supposedly the Office of General Counsel made this
14 decision and I guess I just want to see what was the
15 basis for that decision because I could see that could
16 be applied to AUs, to ANPs, to AMPs also. I would
17 like to see that.

18 MS. FLANNERY: We can certainly supply the
19 basis. I would request that from OGC.

20 DR. NAG: I think knowing the basis would
21 be helpful because now that we have made this
22 recommendation -- a motion, we would like to know what
23 the problems were so that when we make the motion and
24 we double up this motion, we can take into
25 consideration what the problems were.

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1 MR. LEWIS: I think you need to see the
2 basis. I don't see any representatives from OGC here
3 but when we get an internal interpretation from them,
4 they often reply and label it attorney/client
5 privilege. We have to pursue their permission before
6 we can show you the basis. I think that shouldn't be
7 a problem. It's just a fact. It's whatever they
8 found in the rules.

9 CHAIRMAN MALMUD: I think that NRC staff
10 understands our concern regarding the process and
11 hopefully we will get the information needed so that
12 when this motion goes forward on our part it doesn't
13 meet an obstacle that was preventable by our knowing
14 the basis for the prior decision.

15 MR. LIETO: And the other thing, I think,
16 is that there are a lot of licenses out -- I shouldn't
17 say a lot. There are a number of licenses out there
18 that have multiple RSOs listed, in some regions
19 anyhow.

20 Does that mean all these licenses are
21 going to receive sort of "sorry but" type notes from
22 the regions or have the regions been notified that
23 they have to amend all these licenses? I think you
24 are going to get some -- I think you will get some
25 backlash on this. I really do.

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1 CHAIRMAN MALMUD: Thank you. Our motion
2 has been moved, seconded, and discussed. Any further
3 discussion of the motion?

4 MS. SCHWARZ: I was just going to ask one
5 question. I think part of Ralph's concern is that
6 since he had been involved in talking to staff when
7 the decision was made that it was not possible to move
8 forward that he kind of was kept in the loop just to
9 -- you know, then maybe before we got to this point or
10 even before you sent out the list it would allow him
11 to continue possibly moving the effort forward rather
12 than to come to the table. Now it just delays things.

13 CHAIRMAN MALMUD: If I may, I have the
14 memo that was sent to the members of the Committee on
15 January 10th by you. It covers item number -- well,
16 we don't know.

17 PARTICIPANT: Ten.

18 MS. TULL: Is it updated?

19 CHAIRMAN MALMUD: It said it was under
20 consideration and need OGC interpretation.

21 MS. TULL: Okay.

22 CHAIRMAN MALMUD: That was the January
23 10th memo.

24 MS. TULL: Okay. It would have been the
25 next one. They came out in April then.

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1 MS. SCHWARZ: Yes, I saw it in April.

2 MS. TULL: It's hard to differentiate but
3 No. 4 and No. 10 are bolded to indicate that there has
4 been a change basically since last year to this year.

5 CHAIRMAN MALMUD: Once again, is there a
6 vote? All in favor?

7 ALL: Aye.

8 CHAIRMAN MALMUD: Any opposed? Any
9 abstentions? It's unanimous. Thank you.

10 MS. TULL: We'll move on to No. 11.

11 CHAIRMAN MALMUD: Please move forward.

12 MS. TULL: No. 11 says NRC staff should
13 include the three-case work experience requirement for
14 individuals seeking authorization for Y-90 microsphere
15 use; however, the three cases do not have to be with
16 the particular type of microsphere for which the
17 individual is seeking authorization.

18 Furthermore, ACMUI recommends the training
19 and experience does not have to be performed under the
20 supervision of an AU, and NRC staff should replace the
21 proposed supervision paragraph with the existing
22 language from 10 CFR 35.690(c).

23 I'm going to try to break this one up and
24 go through it piece by piece. For the three-case work
25 experience that is currently in the guidance. That

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1 piece is accepted. For the next piece it says it
2 doesn't have to be with the particular type of
3 microsphere. NRC did not accept that piece so if you
4 want to use TheraSphere you need to go get TheraSphere
5 training from MDS.

6 For the third piece, ACMUI recommends the
7 training and experience does not have to be performed
8 under the supervision of an AU. I'm going to give a
9 presentation tomorrow that actually gives two
10 pathways. The first pathway would be under the
11 supervision of an AU as the guidance is currently
12 written. The second pathway will be a little
13 different and would not require AU supervision.

14 For the last piece it says NRC staff
15 should replace the proposed supervision paragraph with
16 the existing language from 690(c). That is accepted
17 and is in the proposed guidance that I will give you
18 tomorrow. Any comments on that?

19 No. 12, NRC staff should delete the
20 attestation requirement for Y-90 microsphere users and
21 incorporate a requirement in the second paragraph of
22 the guidance for individuals seeking authorization to
23 provide and retain documentation of the completion of
24 training. This was Dr. Williamson's recommendation
25 before he left and this was accepted and has been

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1 incorporated into the proposed guidance that you will
2 see tomorrow.

3 No. 13, NRC staff should incorporate the
4 proposed wording for the team approach section of the
5 Y-90 microspheres guidance with one exception: ACMUI
6 recommends the word "oncology" be replaced by "cancer
7 management." This is accepted and is published in the
8 current guidance which was September of '07.

9 No. 14, NRC staff should incorporate the
10 proposed wording that notification under 10 CFR 35.14
11 does not apply for specific medical use licensees.
12 This item was moved to the October agenda and the
13 motion was changed. We'll come to it later on when we
14 get to the October recommendations.

15 No. 15, ACMUI tabled the absorbed dose vs.
16 activity issue for Y-90 microspheres until the next
17 full ACMUI meeting. Again, we will get to that later
18 on in the list.

19 No. 16, NRC staff should revise the
20 current guidance to conclude that the surgical removal
21 of the sentinel lymph node is an independent procedure
22 and should not be regulated by NRC. This RIS has been
23 sent to ACMUI and you provided comments on that.

24 No. 17, NRC staff committed to consult
25 legal counsel to determine the feasibility of

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1 discussing PRM 35-20 (Ritenour/AAPM petition) with
2 ACMUI members in a closed executive session. This was
3 discussed at the last meeting and it's also on the
4 agenda for this meeting for a status update on that.

5 No. 18, NRC staff should arrange a
6 briefing for ACMUI members regarding the Increased
7 Controls Orders to be issued later this year for
8 fingerprinting. This was completed -- I'm sorry. Let
9 me reread it. This was done. Dr. Vetter and Mr.
10 Lieto came to headquarters last year.

11 No. 19, NRC staff should engage ACMUI in a
12 discussion regarding the review of operational events
13 and data and work towards a goal of minimizing
14 therapeutic medical events, if directed by the
15 Commission to do so. The Commission did not direct
16 this. It was pulled out of the Staff Requirements
17 Memorandum so we are not taking any action on this
18 item.

19 Yes, Dr. Malmud.

20 CHAIRMAN MALMUD: I just wanted to make a
21 comment actually that all the Committee members know
22 that I did meet with the Commissioner regarding the
23 issue of fingerprinting. The response from the
24 Commissioner was that this recommendation came from a
25 different authority, a higher authority. Therefore, it

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1 was not in the NRC's purview to challenge it.

2 MS. TULL: For 19 or for 18?

3 CHAIRMAN MALMUD: The fingerprinting
4 issue.

5 MS. TULL: So for 18. Okay.

6 CHAIRMAN MALMUD: Yes, fingerprinting.

7 MS. TULL: All right. For 19 this was
8 with regard to medical events.

9 CHAIRMAN MALMUD: No, I said for the
10 previous item, for the fingerprinting issue.

11 MS. TULL: Okay. We will be discussing
12 that with the Commission. Dr. Vetter is giving a
13 presentation tomorrow afternoon so we will be talking
14 about it again. We'll jump to No. 20.

15 CHAIRMAN MALMUD: No. 20.

16 MS. TULL: NRC staff should provide
17 detailed background information for the current and
18 future presentations on the subject of potential
19 changes to 10 CFR Part 35. It's not on the agenda
20 this time so not an issue there.

21 NRC staff should email the ACMUI members a
22 copy of the memo summarizing action items and motions
23 made during the meeting. I believe everyone has been
24 receiving copies.

25 No. 22, ACMUI supports grandfathering for

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1 individuals who had previously been determined to be
2 trustworthy and reliable and granted unescorted
3 access. This was not accepted and Orders were mailed
4 back in October.

5 For No. 23, ACMUI agrees to assist the
6 NRC, if requested, to determine those levels and types
7 of material that could be of such significance to
8 public health and safety to warrant fingerprinting and
9 background checks. This was not requested of ACMUI
10 but will be discussed tomorrow during the Commission
11 meeting.

12 No. 15, NRC staff should revise the
13 current regulations to include Canadian trained
14 individuals who have passed the ABNM certification
15 exam. This was accepted. I don't know if that was in
16 the January memo that I sent you but it has been
17 accepted since then. We will put this in the User
18 Need Memo and the rulemaking group will consider it.
19 This will be similar for the other types of uses for
20 radiation oncologists. We'll do the same for nuclear
21 medicine.

22 For No. 26, NRC staff should maintain
23 Compatibility B for training and experience
24 requirements to ensure that authorized individuals may
25 cross state borders and practice throughout the U.S.

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1 This is accepted. This is NRC's current practice and
2 will remain that way.

3 No. 27, NRC staff should accept a
4 preceptor statement from another AU for non-board
5 certified individual if the AU who supervised the
6 training and work experience is not available as a
7 preceptor. This is also accepted and is NRC's current
8 practice.

9 For No. 28, NRC staff should add increased
10 complexity vs. additional benefit as an agenda item
11 for the October ACMUI meeting so that ACMUI may
12 continue the discussion on this topic. This was
13 discussed in October.

14 No. 29, the AU should be required to place
15 a signature on orders for radioactive material before
16 the supplier can legally ship the material to an
17 institution. This was a presentation made by Dr.
18 Welsh. The motion did not pass.

19 No. 30, The Elekta Perfexion should be
20 regulated under 10 CFR 35.1000 until 10 CFR 35.600 is
21 modified to be performance-based which would allow the
22 Perfexion to be regulated under 10 CFR 35.600. Dr.
23 Nag has been leading a subcommittee on this and they
24 have provided revisions to 35.600 so we will discuss
25 that later today.

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1 No. 31, NRC staff should require
2 experienced RSOs and AMPs to receive additional
3 training if the individual is seeking authorization or
4 responsibility for new uses. This is accepted and
5 will be put in a User Need Memo for consideration for
6 rulemaking. Any questions?

7 No. 32, NRC staff should not require
8 experienced RSOs to obtain written attestation to
9 become authorized or have responsibility for new uses.

10 This is also accepted and will be in a User Need Memo
11 and will be considered for a rulemaking.

12 No. 33, NRC staff should not revise 10 CFR
13 35.75 to read "5 mSv/year (0.5 rem/year)." This was
14 not accepted and a RIS was emailed to ACMUI on April
15 1st and rulemaking will proceed on this. Any comments
16 or questions there?

17 DR. NAG: One other instance perhaps what
18 exactly does that mean.

19 MS. TULL: Dr. Vetter.

20 DR. VETTER: This has to do with the
21 release of patients containing radioiodine,
22 radiopharmaceutical, or an implant and they are
23 allowed to be released on the basis of the fact that
24 the calculations show a member of the public did not
25 receive more than .5 rem.

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1 If you go back to the guidelines from NCRP
2 and others, ICRP and so forth, those are annual limits
3 and the regulations aren't extremely specific on that
4 and I think this is an attempt by NRC to make it more
5 specific that a member of the public should not get
6 more than .5 rem per year from the release of these
7 patients. It's going to be difficult in some cases to
8 implement.

9 I haven't heard a lot of discussion about
10 this in the professional community but you can't
11 always tell when a patient has to come back and have
12 more radioiodine and they are going to go back to the
13 same family. Patient calculations, first of all, are
14 very conservative.

15 The research that has been published show
16 that these caretakers don't get near the .5 rem so
17 there is room, I think, in there for retreating
18 patients and still being within the limit of .5 rem
19 per year. Exactly how we would account for that I
20 don't think has been worked out very well yet.

21 DR. NAG: My question if it has not been
22 accepted what is the implication of that? I mean,
23 let's assume we find that it does go to .5 rem. What
24 is the impact of this application? Does that mean
25 that patient cannot have anymore applications for that

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1 year?

2 DR. VETTER: They would have to be
3 hospitalized.

4 MS. TULL: They can't be released.

5 MR. LIETO: There's also a practical
6 implication that I think Dr. Vetter was getting at is
7 that some patients don't come back to the same place
8 for treatment or may go to a different facility. You
9 have to set up a mechanism to be sure that you have
10 researched what previous treatments that individual
11 has gotten for release as well as other procedures
12 because it's not just for therapeutic.

13 The release is for any radionuclide
14 administration. If the patient had cardiac studies
15 and was released, you are going to have to go back and
16 say they had a therapeutic application and were
17 released. This is going to set up a requirement for a
18 lot of paperwork and documentation that has never been
19 required in past applications.

20 Also there are some new treatments that
21 are coming out where there are multiple therapeutic
22 treatments given over the course of the year and might
23 either preclude all those be given or that they all
24 would have to be set up such that the patient is
25 hospitalized for each of those treatments. There was,

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1 I think, some valid concerns about not increasing this
2 or leaving the time specification off.

3 I had kind of a note this was another one
4 of the situations where a decision was made not to do
5 it but the reasons, the basis for not accepting the
6 Committee's recommendation, I mean, you don't hear
7 about until you come out with a RIS that is sent to
8 everybody. I think that would have been nice to kind
9 of know what the basis for not accepting the
10 Committee's recommendation would have been prior to
11 sending something out to all licensees.

12 MR. LEWIS: We researched the regulatory
13 history behind this particular rule and it was clear
14 in that regulatory history that we always intended per
15 year for this release so we viewed the regulation as
16 always having been per year but somewhat ambiguous.
17 This is viewed mainly as a clarification of an error.

18 That is what we explained in the RIS. You
19 are right, though, that there is some implementation
20 question. I want to be clear, though, this is the
21 dose to other people, not to the patient. Some
22 additional patient instructions or questions may be
23 warranted in order to implement this on a case-by-case
24 basis.

25 The international foundation for this

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1 regulation was clear. The intent in our statement of
2 considerations was clear and the people that actually
3 wrote the rule their intent was clear. We view this
4 not as a change in policy but as a clarification that
5 this has always been the policy.

6 CHAIRMAN MALMUD: Dr. Nag.

7 DR. NAG: Could I request that when a
8 motion has been passed by the ACMUI and for whatever
9 reason it is not accepted, for any valid reason why it
10 is not accepted, if something is not accepted there is
11 a separate notification of that rather than bundling
12 the whole thing into one because most of these we
13 assume have been accepted but if something is not
14 accepted, we would probably like to know that. Could
15 we request something like that from the NRC?

16 MR. LEWIS: That's fair enough.

17 MS. TULL: Sure.

18 CHAIRMAN MALMUD: Would you like to make a
19 motion?

20 DR. NAG: Yes. I would make a motion that
21 if an ACMUI recommendation has been deemed not
22 acceptable by the NRC, that information be
23 communicated directly to the members of the ACMUI as a
24 separate memo.

25 CHAIRMAN MALMUD: You want to insert the

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1 word promptly in there?

2 DR. NAG: Promptly. As soon as it is
3 known.

4 CHAIRMAN MALMUD: Is there a second to the
5 motion?

6 DR. WELSH: Second.

7 CHAIRMAN MALMUD: Dr. Welsh seconds the
8 motion. Any discussion of the motion? All in favor
9 of the motion? Any opposed to the motion? Any
10 abstentions? It's unanimous. Thank you.

11 MS. TULL: All right. We'll move to No.
12 34.

13 CHAIRMAN MALMUD: Thank you.

14 MS. TULL: No. 34 reads, NRC staff should
15 modify 10 CFR 35.491(b)(2) to specify "superficial"
16 ophthalmic treatments. Additionally, NRC staff should
17 change the title of 10 CFR 35.491 to specify
18 "superficial" ophthalmic treatments.

19 I think NRC agrees that changes need to be
20 made and that there will be modifications. We haven't
21 come up with any specific wording for this. It's not
22 in the current rulemaking but as this is developed it
23 will be sent to ACMUI. There will be a public comment
24 period that we always see. You will have an
25 opportunity to see this.

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1 For No. 35, NRC staff should not revise 10
2 CFR 35.491 which was intended for ophthalmologists to
3 include training and experience for the new
4 intraocular device. Instead, NRC staff should
5 regulate the new intraocular device under 10 CFR
6 35.490. Same thing on this. We are still going to be
7 working on some words when rulemaking comes around.

8 No. 36, NRC staff should not require
9 medical licensees regulated under 10 CFR 35.400, 500,
10 or 600 as applicable to only use the sealed sources
11 and devices for the principle use as approved in the
12 SSDR. This is accepted and is in progress. I'm
13 assuming it will be considered in rulemaking.

14 No. 37, NRC staff should revise 10 CFR
15 35.290 to allow physicians to receive training and
16 experience in the elution of generators and
17 preparation of kits under the supervision of an ANP.
18 This is accepted and will be considered in a User Need
19 Memo for rulemaking.

20 No. 38, NRC staff should revise the
21 microsphere guidance to allow the written directive to
22 include either "dose to target tissue (Gy or rad)" or
23 "activity administered (mCi or GBq)." This is
24 accepted and is in the current proposed guidance that
25 is in your binders we will discuss tomorrow.

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1 No. 39, NRC staff should revise the
2 microsphere guidance to include a paragraph
3 referencing medical event reporting for microsphere
4 use. (10 CFR 35.3045). This is accepted and is in the
5 proposed guidance for discussion tomorrow.

6 No. 40, NRC staff should revise the
7 microsphere guidance to reinsert the proposed
8 paragraph with modification. The paragraph should
9 state, "Procedures for administrations requiring a
10 written directive should, for yttrium-90 microsphere
11 administration, be performed in accordance with the
12 written directive." This is accepted and is in the
13 current guidance that will be proposed tomorrow.

14 No. 41, NRC staff should revise the
15 microsphere guidance to allow an experienced AU for
16 the medical use of a certain type of microsphere to
17 become an AU for the medical use the same type of
18 microsphere on a different license, similar to the
19 notification provision in 35.14. This is accepted and
20 is in the proposed guidance for tomorrow.

21 No. 42, NRC staff should revise the
22 microsphere guidance to add a paragraph which states,
23 "training in manufacturer's procedures, commensurate
24 with the individual's duties to be performed, must be
25 provided to individual preparing, measuring,

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1 performing dosimetry calculations, or implanting
2 microspheres." This is accepted and is in the
3 proposed guidance that will be presented tomorrow.

4 No. 43, NRC staff should revise the
5 microsphere guidance to read, "The written directive
6 should include after implantation but before release
7 of the patient from licensee control: the radionuclide
8 (including the chemical/physical form [Y-90
9 microspheres]), the manufacturer, treatment site, and
10 the total dose or administered activity.

11 I say this is partially accepted. There
12 is a statement very similar to this in the proposed
13 guidance and we will go over it in detail tomorrow.
14 We have added some other new things so I don't want to
15 say totally accepted on this because we have fit some
16 new pieces in that I want to discuss with everyone.
17 We are definitely on the same page and moving in the
18 same direction.

19 No. 44, ACMUI recommended for each
20 training program, including radiology, radiation
21 oncology, radiation physics, and nuclear pharmacy,
22 that the curricular requirements be established by
23 those boards, which recognize the importance of the
24 NRC standards for radiation safety and radiation
25 physics. This was not accepted and the comment here

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1 was that NRC sets general topics and a minimum number
2 of hours. We are really only focusing on the
3 radiation safety and not all curricular topics. Any
4 comments or questions?

5 CHAIRMAN MALMUD: That was an important
6 issue in the minds of the Committee members who were
7 concerned about the logic in the requirement of
8 specific numbers of hours for various specialties.
9 Therefore, the Committee members were puzzled as to
10 how the numbers were derived.

11 Analogies were drawn between a university
12 course that might be offered in the fall or spring
13 semester and its number of hours compared to the
14 numbers of hours required in specific topics by the
15 NRC. Does that summarize the subject well?
16 Therefore, we remain puzzled.

17 Dr. Vetter.

18 DR. VETTER: Yeah, Vetter. I think that
19 does summarize it. I would underscore boards. In
20 other words, the Committee felt the boards were in a
21 better position to know what is going on in the field
22 than the NRC staff knows and the staff are setting the
23 numbers. The boards would have a better feel for what
24 the thing ought to be about and how much training in
25 each area. I guess that might be helpful to

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1 underscore boards.

2 CHAIRMAN MALMUD: You are correct.

3 DR. VETTER: We are asking that the boards
4 actually set the amount of training that should be
5 required. Then if a person takes that material and
6 studies that material, gets those number of hours,
7 passes the boards, they become certified through the
8 certification route, that is sort of a long-term view
9 on how we think that should look. Otherwise, it
10 appears as the field as been changing that the hours
11 are somewhat arbitrary. What exactly do those hours
12 mean?

13 CHAIRMAN MALMUD: Thank you for clarifying
14 that, Dr. Vetter. Essentially the Committee had no
15 objection to the NRC establishing topics that should
16 be covered by the board. The objection was to the
17 number of hours specified by the NRC of the board in
18 specific topics. They range from being quite
19 reasonable to being excessive.

20 The reason the challenge is to the
21 excessive number of hours is that the boards currently
22 in their training programs are teaching residents,
23 particularly in the field of radiology technologies
24 that did not exist only a few years ago and,
25 therefore, there is a time limit as to how much time

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1 can be given to each subject.

2 Therefore, each subject should have a
3 logical basis for the number of hours devoted to it.
4 The number of hours currently identified by the NRC
5 defy logic and defy their rationalization by
6 professional educators. That was the challenge as I
7 understood it. Am I expressing the Committee's
8 feelings well?

9 DR. VETTER: Yes.

10 CHAIRMAN MALMUD: Here you have a
11 committee that serves the NRC which is made up of a
12 number of professional educators in the fields of
13 radiologic technology at all levels who feel very
14 consistently and uniformly and unanimously that the
15 number of hours established by the NRC, not the topics
16 but the number of hours, is illogical and in some
17 situations excessive to the point of absurdity.

18 Yet, the opinion of educators whose lives
19 are devoted to these topics are rejected. It is a
20 challenge to our understanding. That is the feeling
21 of the Committee.

22 Cindy, did you raise your hand?

23 MS. FLANNERY: Just to point out that Ron
24 has a question.

25 DR. ZELAC: Ron Zelac. I'm a little bit

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1 puzzled by the position to the extent that there is
2 not for the board certification pathway certainly a
3 specificity as to how many hours have to be spent for
4 each of the various topics. It's the totality over
5 the whole range of topics which is required. We are
6 totally basically for 290 and 390. Is there a basic
7 problem with the total number of hours? Is that what
8 you're telling us? The 700 hours is too high, too
9 low, or should be indeterminant?

10 CHAIRMAN MALMUD: It should be
11 indeterminant and it should be a decision made by the
12 educators with respect to how much time should be
13 spent on each particular subject.

14 DR. ZELAC: Then what about the alternate
15 pathways? There have to be alternate pathways for
16 people that are not becoming board certified or have
17 not yet received board certification.

18 CHAIRMAN MALMUD: That is how the issue
19 arose because there is a de facto intrusion of the NRC
20 into the educational process by creating numbers for
21 the alternate pathways, numbers of hours for the
22 alternate pathways when at least 20 percent of those
23 who are going to be finishing their training program
24 will not have been board certified when they enter
25 practice for the first several years, the first year

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1 or two.

2 DR. ZELAC: The real objection then is to
3 the numbers of classroom and laboratory hours that are
4 specified in the alternate pathway basically, not to
5 the total number of hours.

6 CHAIRMAN MALMUD: That is exactly correct.
7 Dr. Zelac, you are correct.

8 DR. ZELAC: As was pointed out earlier, by
9 Ashley in this discussion, those numbers in terms of
10 numbers of classroom and laboratory hours that appear
11 in the regulations were a compromise. They were a
12 compromise from the positions of the Advisory
13 Committee and the Agreement States who are at opposite
14 poles.

15 At the time that this compromise was
16 reached, both the Agreement States and the Advisory
17 Committee were asked if they could live with this
18 compromise and the response from both was, "Yes, we
19 understand it's a compromise but we are willing to go
20 along with it." What I am basically hearing now is
21 that the Advisory Committee at this point is not
22 willing to go along with this any longer.

23 CHAIRMAN MALMUD: The Advisory Committee
24 objects to it. I would hesitate to say it won't go
25 along with it but it objects to it.

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1 Mr. Lieto.

2 MR. LIETO: Well, I guess maybe my memory
3 is a little bit different of this compromise. The
4 Committee did not compromise on the number of hours
5 that it had recommended for the alternate pathway.
6 The compromise was that we were told that in a
7 discussion that occurred with NRC and the Agreement
8 States the number of hours that had been reached this
9 never went out for public comment and further
10 discussion.

11 It just came down that was going to be a
12 compromise because there needed to be a fixed number
13 of hours for consistency across the Agreement States
14 and NRC so that there was this transparency of
15 adequate training and experience via the alternate
16 pathway.

17 I think the problems with this, and this I
18 think is a large part of Dr. Eggli's discussion for
19 the Commission in his presentation, is that this
20 alternate pathway has become the de facto training for
21 residents in order to get board certification. It has
22 become the end all and be all that was never intended
23 to be. Alternate pathway was always intended to be
24 sort of that mechanism. If you didn't get board
25 certification, this is the way you went.

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1 It has now become actually the training
2 and experience requirements for the boards and for the
3 residents to get board certification. I think the
4 number of hours that have gone into this have become
5 very, very prescriptive and I think this is where the
6 renewed objections are arising from.

7 CHAIRMAN MALMUD: There was flexibility
8 from the NRC in its interpretation of what these
9 number of hours represented with respect to classroom
10 hours versus experiential hours in the laboratory in
11 the clinic. The prescription of numbers of hours
12 remains and it is a thorn in the side of the members
13 of the ACMUI.

14 MR. LEWIS: Dr. Malmud, can you clarify
15 for me, or someone on the Committee, is the Committee
16 advocating a regulatory change or a guidance change
17 because the regulation is very clear about the 700
18 hours but I'm kind of hearing a mixed message about
19 whether that is sufficient and it is the implementing
20 guidance or whether that in and of itself is the
21 problem.

22 CHAIRMAN MALMUD: Mr. Lieto, would you
23 care to address that?

24 MR. LIETO: I didn't mean to steal your
25 thunder from earlier but I think the emphasis is how

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1 the NRC is recognizing the boards. This relates to
2 the board recognition aspect, if I'm not mistaken
3 about this agenda item, this recommendation item No.
4 44. It is not meant as an alternate pathway.

5 It's how boards are being evaluated and
6 the boards need to be allowed the flexibility to
7 adjust their training and experience based on the
8 needs for the training programs. The hour
9 requirements really I think are pretty much the same
10 as they were in the '80s and so it just needs to be --
11 they just need to be allowed I think that ability.
12 They are tied into more of the educational needs of
13 the physicians in order to practice competently. I
14 think that is where it's right. I don't think it's
15 meant to just address the alternate pathway.

16 CHAIRMAN MALMUD: Anyone else wish to
17 comment? Dr. Vetter.

18 DR. VETTER: Just a philosophical remark.
19 If we go back to when Part 35 was first revised and
20 we were supposed to put together some recommendations
21 relative to training requirements, several times the
22 Committee made the point that sitting in a classroom a
23 certain number of hours does not determine knowledge.
24 Passing a board exam is a measure of knowledge.

25 So consistently we have tried to emphasize

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1 that for us the boards having a workable pathway to
2 get board certified as soon as possible after training
3 is the best way to determine that the physician or the
4 physicist or whomever has knowledge. Sitting in a
5 classroom 200 hours doesn't demonstrate knowledge.
6 That's where we get hung up on the number of hours.

7 We are not saying 200 is wrong but we
8 think the people who are in a better position to
9 determine those numbers of hours are the people who
10 are in practice and that would be the boards who are
11 in practice who have a good understanding of what kind
12 of knowledge is necessary in order to have a good
13 practice, good safe practice. It is a philosophical
14 thing that we would really emphasize a good strong but
15 workable board pathway. Get people board certified as
16 soon as possible.

17 CHAIRMAN MALMUD: Thank you, Dr. Vetter.
18 I think in summary there were two issues. One was the
19 one you just raised which is the issue of the board's
20 competency to test for this knowledge.

21 The other one was the perhaps unintended
22 consequence but the outcome which was the ultimate
23 pathway since it is the pathway for about 20 percent
24 of the residents completing training annually
25 including those who are going to take the boards and

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1 those who have failed the boards and are going to take
2 them again becomes an issue of having established a
3 number of hours required training under the alternate
4 pathway for one in five individuals.

5 Therefore, the boards must address those
6 numbers of hours to meet the requirements of the NRC
7 for those who will not have passed the boards in the
8 first several years after graduation. That is how the
9 issue arose. Thank you. Move on.

10 MS. TULL: No. 45, ACMUI should form a
11 subcommittee to address issues with 10 CFR 35.600 as
12 they relate to the Elekta Perfexion. The subcommittee
13 includes: Dr. Nag, Dr. Thomadsen, Dr. Welsh, and Mr.
14 Lieto. The subcommittee should consult with Ms.
15 Gilley on behalf of the Agreement States; the vendor;
16 the American Society for Therapeutic Radiology and
17 Oncology; and the AAPM. This is in progress and we
18 will hear a subcommittee report later today.

19 No. 46, ACMUI should form a subcommittee
20 to further discuss the proposed change to 10 CFR 35.75
21 to release patients, if the total effective dose
22 equivalent to any other individual from exposure to
23 the released individual is not likely to exceed 5
24 mSv/year. The subcommittee includes: Dr. Vetter, Dr.
25 Eggli, and Dr. Fisher. The subcommittee reported back

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1 to us last October, the next day. The second day of
2 the meeting they reported back to us.

3 CHAIRMAN MALMUD: Thank you. May I just
4 ask the members of the Committee who practice at
5 hospitals whether they are physicians or other
6 professionals, are you aware that your hospital allows
7 patients who are radioactive to remain overnight? In
8 other words, do your hospitals allow the treatment
9 with I-131 of in-patients?

10 Mine no longer allows it. That's why I
11 was asking the question. That means in most hospitals
12 the therapy would not be denied simply because the
13 patient had to be isolated overnight. That's good
14 news. I'll have to transmit that back to our own
15 hospital. We used to be allowed to do it but somehow
16 it seems to have disappeared.

17 Sally.

18 MS. SCHWARZ: What is the reason that they
19 stopped?

20 DR. NAG: Money.

21 CHAIRMAN MALMUD: The reason is that it
22 requires the use of a private room with restriction of
23 the patients in the adjacent rooms under certain
24 situations. The nursing staff in particular is very
25 concerned about radiation exposure to themselves and

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1 to other workers in the hospital.

2 They are most distressed when the patient
3 has a urinary catheter with the collection of
4 radioactive urine in the room. They are concerned
5 about the radiation to them and the handling of the
6 bodily fluids of these patients in addition to serving
7 the patient's needs medically. It relates to the
8 staff.

9 MS. SCHWARZ: What alternative does the
10 patient have?

11 CHAIRMAN MALMUD: Under our current
12 practices we are allowed to treat the patients and
13 send them home. It is unusual to require I-131
14 therapy for an in-patient because I-131 therapy -- I'm
15 speaking now of thyroid cancer -- is not a therapy
16 which is effective within several days.

17 It is only a therapy which has a large
18 radiation burden associated with it for several days
19 until the excretion of the I-131. Most of these
20 patients can be treated at home. I really have to do
21 some homework to find out why our hospital policy
22 changed because it wasn't that way when I was still
23 practicing as Chief of Nuclear Medicine but it has
24 changed subsequently. I suspect it has to do with the
25 economics of it.

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1 DR. NAG: Yes, I would assume that your
2 hospital then does not permit low dose rate
3 brachytherapy. Low dose rate brachytherapy in the
4 hospital is usually three days.

5 CHAIRMAN MALMUD: It's my understanding
6 that the hospital does.

7 DR. NAG: But it should be similar then.

8 CHAIRMAN MALMUD: I don't know what caused
9 the change.

10 DR. VETTER: There are some reimbursement
11 issues. Occasionally the doctor has to clear it with
12 the insurance company prior to treatment.

13 CHAIRMAN MALMUD: Thank you. I'm
14 reassured, though, that the majority of hospitals, at
15 least represented by this Committee, does allow in-
16 patient treatment.

17 Thank you. Please go on. I'm sorry for
18 the interruption.

19 MS. TULL: That's okay. No. 47, NRC staff
20 should set up NMED accounts for new members and reset
21 passwords for other members as needed following the
22 October meeting. This was completed. I believe
23 everyone has access to NMED with the exception of Mr.
24 Mattmuller. I will get you set up on that after this.
25 I wanted you to know what NMED was all about first.

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1 It's very exciting.

2 MR. MATTMULLER: Thank you. That's what
3 Sally told me.

4 MS. TULL: No. 48, NRC staff should add an
5 item to the spring 2008 agenda for Dr. Thomadsen to
6 provide a presentation to ACMUI members and NRC staff
7 on the causes of medical events. Dr. Thomadsen's
8 presentation will also provide suggestions for
9 questions NRC should ask to receive more accurate
10 information on the causes of events. Dr. Thomadsen
11 will be giving us a presentation later today.

12 No. 49, ACMUI should form a subcommittee
13 to annually review byproduct material events, perform
14 analysis, and report to the full Committee. NMED data
15 should continue to be presented to ACMUI at the fall
16 meetings, and the subcommittee should analyze the data
17 presented at the fall meeting in order to provide a
18 full report at the spring meeting.

19 The subcommittee includes: Mr. Lieto as
20 the chair, Drs. Nag, Thomadsen, and Suleiman. The
21 subcommittee will consult with an Agreement State
22 representative, Ms. Gilley, and designated NRC staff
23 as appropriate. We will hear from Mr. Lieto on the
24 ACMUI subcommittee report on medical events later
25 today.

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1 No. 50, ACMUI byproduct material events
2 subcommittee should publish reports as necessary to
3 ensure end-users receive the message. That is at the
4 discretion of the subcommittee so I will leave that
5 open and ongoing for you to decide.

6 No. 51, ACMUI recommends a subcommittee
7 comprised of Dr. Vetter and Dr. Nag to make comments
8 and recommendations on behalf of the entire ACMUI in
9 terms of the medical implications of the upcoming
10 National Academies of Science study, which is in
11 response to provisions of the 2005 Energy Policy Act.

12 This is a presentation that Rob Lewis is
13 going to give next and Dr. Nag provided a letter on
14 behalf of ACMUI in consultation with Dr. Vetter before
15 he left the country. Everyone should have a copy of
16 those comments the ACMUI provided. The letter was
17 sent to Congress.

18 Any questions or comments on any of the
19 items?

20 CHAIRMAN MALMUD: The Committee thanks
21 Ashley Tull for an yeoman's job on presenting these 51
22 items.

23 MS. TULL: You're welcome. We'll do it
24 again at the end of the meeting.

25 CHAIRMAN MALMUD: We look forward to it.

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1 MS. TULL: All right. I'm handing out the
2 presentation that Rob Lewis is going to give. These
3 are the slides right now because he's about to start.

4 DR. NAG: Mr. Chairman.

5 CHAIRMAN MALMUD: Yes.

6 DR. NAG: The ACMUI had made a
7 recommendation about permanent brachytherapy ruling
8 though it was given through the NRC staff. The NRC
9 has now given their initial -- I guess all of you have
10 received the initial memo from the NRC on permanent
11 brachytherapy. I think it's about to be implemented
12 but it did not come back to the ACMUI.

13 There was some misinterpretation made, or
14 I think there was a misinterpretation made about what
15 the ACMUI said and how it was implemented by the NRC
16 during the rulemaking. I think this is a matter I
17 would like discussed in the ACMUI before the permanent
18 brachytherapy ruling becomes effective. I think there
19 are some major concerns that I have and that members
20 of the Radiation Oncology community has.

21 CHAIRMAN MALMUD: Dr. Nag, are you
22 prepared to raise that issue at this meeting?

23 DR. NAG: If need be I am prepared to
24 address what the problems are.

25 CHAIRMAN MALMUD: Thank you. Can we

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1 squeeze that into the agenda, Cindy?

2 MS. FLANNERY: I'm not certain we would be
3 able to do that. I think the only time that we have
4 available would be on the second day after the
5 Commission meeting at 3:00. My concern there is I
6 don't know if people have flights and were expecting
7 to be out of here at 3:00.

8 The other option I can throw out is to
9 have a separate teleconference at a future date. I
10 guess it's up to you as a committee depending on what
11 your schedules are for flights back.

12 DR. NAG: This morning I have two
13 presentations and I think I have a total of one hour
14 and 15 minutes for both of them. They are very simple
15 and straightforward so with that I request that if the
16 presentations are made and all the questions are
17 answered in less than that one hour and 15 minute
18 time, I at least be allowed to present what I think
19 are problems with the permanent brachytherapy
20 rulemaking that is going on.

21 CHAIRMAN MALMUD: If Dr. Nag can present
22 his material within the time allowed today, would that
23 be acceptable? It is to the Chair if it is acceptable
24 to you.

25 MS. FLANNERY: I guess I just want to make

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1 sure I understand this right. Are you shortening your
2 time or are you getting --

3 DR. NAG: I think the amount of time that
4 has been allotted there, I think I can give my
5 presentation in way less time than that. I don't want
6 to make short the presentation but if whatever needs
7 to be discussed can be discussed in less than the one
8 hour and 15 minutes, and I think in about 40 minutes
9 or so. I don't have that much to say so unless there
10 are a lot of additional questions, I think 45 minutes
11 should be enough for both of those.

12 MS. FLANNERY: Okay. That's fine by me.

13 DR. NAG: It seems very straightforward
14 the two presentations I have.

15 CHAIRMAN MALMUD: Then there is agreement
16 that if you can contain it within the time allowed for
17 your presentations it will be welcomed. Thank you.

18 MS. FLANNERY: And if that doesn't work
19 out, as I said, the backup option is we could schedule
20 a future teleconference.

21 DR. NAG: Or I could at least present what
22 I think the problems are and we could have a separate
23 teleconference to discuss how to solve the problems.
24 I don't think we will be able to solve the problem in
25 a short time.

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1 CHAIRMAN MALMUD: Thank you. We will look
2 forward to hearing that within the time allowed for
3 your presentation.

4 It is now 10:13 and Ashley's presentation
5 has allowed us to move to the next item on the agenda.

6 You have some slides to present?

7 MS. FLANNERY: Do we have a break right
8 now?

9 CHAIRMAN MALMUD: You want to do the break
10 first?

11 MS. FLANNERY: That was on the agenda.

12 CHAIRMAN MALMUD: Break first. Okay.
13 Thank you. We'll take a break first.

14 (Whereupon, at 10:12 a.m. off the record
15 until 10:33 a.m.)

16 CHAIRMAN MALMUD: Thank you, if we may
17 we'll resume now, it being 10:35. And the item on the
18 agenda will be the brief presentation by Rob Lewis.

19 MR. LEWIS: Thank you, Mr. Chairman. I'm
20 joined at the table by Tony Huffert, from our Office
21 of Nuclear Regulatory Research, who is the Project
22 Manager for this effort and our offices, along with
23 the Office of Nuclear Security and Incident Response,
24 have been working together on the NRC's activities and
25 follow-up of this study and the other studies that are

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1 ongoing.

2 The National Research Council of the
3 National Academies, of course, published in February a
4 report dealing with radiation source use and
5 replacement and specifically, alternative technologies
6 that may be suitable to replace radiation sources
7 where they're being used. The effort was started in
8 July of 2006 under a grant from the NRC and the
9 National Academies' effort is one of three efforts
10 that have been ongoing that were mandated by the
11 Energy Policy Act of 2005.

12 There are similar technologies efforts
13 underway by the Energy Policy Act Task Force which is
14 represented by 14 different federal agencies and two
15 state organizations, and also by the Department of
16 Energy. They each produce reports related to
17 alternative technologies to radiation sources.

18 The report, reviewed current industrial
19 research, commercial and medical uses of radiation
20 sources and identified approaches to replace those
21 sources with lower risk alternatives. There are five
22 recommendations in the NAS report. Four of them are
23 to government and one of them is to a professional
24 society.

25 Before I go any farther, I would like to

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1 thank the efforts of Dr. Vetter and Dr. Nag
2 especially, who looked at the issue on behalf of the
3 Committee operating as a sub-group and gave us very
4 quick comments that really helped us communicate the
5 messages that are in the NAS report, especially the
6 impacts of those recommendations upon the practice of
7 medicine.

8 The National Academies' report has, as I
9 said, five recommendations. I'll walk through each of
10 those recommendations very quickly. The first
11 recommendation is just acknowledgment that radiation
12 sources are important to the nation's health, safety
13 and economic health, and replacement of any such
14 sources should proceed with caution, assuring that the
15 functions are preserved that those sources provide.
16 This NRC is really viewing this recommendation as a --
17 as a cautionary note to move forward slowly in any
18 follow-up activities related to the NAS or the other
19 efforts underway.

20 The next recommendation is -- the finding
21 is that the NRC ranks hazards in source security based
22 upon deterministic health effects, prompt fatalities
23 related to the misuse of the radioactive sources, and
24 the Committee felt that NRC should also consider the
25 potential of the sources if they were misused to cause

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1 economic and social disruption. This is the only
2 recommendation that the Committee made that's specific
3 to NRC, asking NRC to take an action. And the
4 corollary recommendation, of course, is the NRC should
5 not confine itself to Category 1 and 2 sources as
6 defined by the IAEA's Code of Conduct. That's the
7 basis of our increased controls orders and other
8 security measures that we've issued that relate to
9 providing additional security to radioactive materials
10 in the last several years.

11 The third recommendation I want to spend a
12 little more time on because that recommendation is and
13 findings and recommendation are the most -- have the
14 most bearing upon the medical industry. The findings
15 are that cesium chloride is a greater concern than
16 other sources and that cesium chloride should be
17 replaced in the U.S. and to the extent possible,
18 elsewhere. And they also went on to find that
19 alternative technologies do exist, be they other
20 nuclides or non-radioactive alternatives such as x-ray
21 devices. And government action is required to
22 implement the replacements because the alternatives
23 cost more and the -- in the infrastructure to use the
24 sources is already well-established and been in place
25 many years.

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1 There are about 1100 blood or research
2 irradiators being used around the country and at about
3 650 locations. And they've been used for many, many
4 years. Of course, the half-life of cesium is 30 years
5 so the device requires very little maintenance, just
6 some of the moving parts require maintenance.
7 They've, in many cases, paid the initial capital cost
8 off long time ago, so the machine is just -- is very
9 economical to retain and continue using and the very
10 reliable technology for research and for blood
11 irradiation in hospitals.

12 The recommendation that the Committee
13 made, however, is the Government should eliminate
14 Category 1 and 2 cesium chloride sources in the U.S.
15 and to the extent possible elsewhere. The Committee
16 felt that cesium, because of its disbursability
17 primarily warranted closer attention than the other
18 nuclides that they looked at and it's on a tier by
19 itself. They looked at international experience and
20 some other countries have already made an effort to
21 move away from cesium chloride and they thought it
22 would be good national policy for us to do so as well.

23 What the NAS committee did not do, though,
24 is they gave the what, you know, the lighthouse. They
25 didn't tell how or who or how -- you know, the

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1 implications. They left that up to the government as
2 a whole to determine what's the best path forward.
3 They did suggest three specific actions. First of
4 all, to discontinue licensing new cesium chloride
5 irradiator sources and their point there is don't
6 exacerbate an existing problem by letting out more
7 sources regardless of how low the numbers may be,
8 because technologies do exist that could be an
9 alternative.

10 The second is put in place incentives for
11 decommissioning the sources. Like I said, the sources
12 have been out and in use for many years. Often
13 there's no incentive for the hospital or research
14 facility to buy a new piece of equipment, whether it
15 be x-ray or cobalt or another form of cesium. There's
16 no economic incentive to get rid to the source. It's
17 working fine for their purposes. And prohibit the
18 export of cesium chloride sources to other countries.

19 This measure is, for example, if the U.S. were to
20 take action to increase the security domestically for
21 cesium chloride sources -- specific to cesium chloride
22 sources, we don't want to create a situation where
23 people start buying an alternative and send the cesium
24 chloride sources to a developing country and our
25 overall world or domestic security overall might

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1 actually decrease.

2 Finding 4 is very similar to one of the
3 findings in Part 3. Basically, the Committee is
4 recognizing that incentives need to be in place to
5 phase out the sources. Market incentives, regulatory
6 incentives, certification incentives, and they're very
7 -- they offer a lot of ideas in the report about
8 things the various Federal Agencies could do to
9 incentivize people replacing their existing sources.
10 And they did note the as our regulations are currently
11 structured, we don't require financial assurance for
12 decommissioning to ensure the source at the end of its
13 life has a disposition solution and they also
14 recommend that we explore providing that type of
15 situation.

16 And the final recommendation, I can speak
17 more about. I'll just briefly mention it here because
18 it, as far as I know, has no bearing upon the medical
19 field. For well-logging, they really think that after
20 cesium, the next nuclide that warrants attention of
21 all the Code of Conduct nuclides is americium.
22 Americium is used a lot in the well-logging industry
23 to determine where to drill basically logging wells
24 and there are alternatives that exist, neutron sources
25 primarily, tritium flows in California. The NAS panel

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1 thinks that the industry need to further define those
2 sources and bring those alternatives back to the state
3 of the art with regard to calibrating which wells to
4 bring in, because it's a big investment decision of
5 where to dig, for example.

6 The NRC has, as I mentioned, we have taken
7 the recommendations. They are what they are. We're
8 going to move forward with the recommendations and our
9 primary vehicle to move the issues forward is the
10 established NRC and Interagency Policy Act task force.

11 As I mentioned, there's 14 different federal agencies
12 represented on the task force. It's not just
13 regulatory. It's the broad suite of all federal
14 activity and there are two state organizations because
15 of course, these issues bear upon Agreement States as
16 well. And the task force has specific subgroups that
17 are active; a subgroup on radiation sources that will
18 consider the social economic aspect that the NAS
19 Recommendation 2 mentioned. There's a subgroup on
20 cesium chloride specifically. They have a product due
21 in the fall.

22 There's a subgroup on public education,
23 which is somewhat unrelated to the NAS finding and
24 finally, there's a subgroup specific to alternative
25 technologies maybe even beyond cesium but all

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1 alternative technology sources. It also has a product
2 due about a year from now. All of those efforts, as I
3 said the NAS told us what, what their opinion is of
4 what should be national policy and the Energy Policy
5 Act is the best vehicle we have to both get a U.S.
6 Government-wide opinion of what the national policy
7 should be and also the how. Who should do things and
8 which things are within the rules and responsibilities
9 of the various agencies and who should do them when,
10 what time frame should they all be done.

11 The -- I did want to mention that there is
12 also alternative technologies work being done by the
13 Environmental Protection Agency. They have an entire
14 project on this. As far as I know, they haven't come
15 out with a view on the NAS findings.

16 MR. HUFFERT: Not yet they haven't.
17 They've been focusing on the lower activity sources
18 today.

19 MR. LEWIS: And the Department of Defense
20 is also looking very closely at the issue, especially
21 with regard to cesium chloride sources and we expect
22 that they may come out with a report related to this
23 in the near future. What the NRC is looking for and
24 we already have some of it from the Committee and we
25 thank you for that, is we need help determining the

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1 impacts, impacts to medical care, impacts, cost
2 impacts of new regulations or regulations to phase
3 things out. And the task force is going to be seeking
4 help from the industry on determining those impacts
5 and the magnitude of them.

6 That's all I had for prepared comments.
7 Thank you once again for your view and comment.

8 CHAIRMAN MALMUD: Thank you, Rob. Tony,
9 did you want to make any comments?

10 MR. HUFFERT: Not at this time.

11 CHAIRMAN MALMUD: Thank you. Dr. Vetter?

12 DR. VETTER: Could you review for us the
13 line of authority here. I mean, the National Academy
14 of Sciences doesn't have any authority over the NRC.

15 MR. LEWIS: That's correct. They simply
16 made a recommendation. The report was delivered to
17 NRC and we passed it onto Congress. That's what was
18 required by the Energy Policy Act. Congress is going
19 to consider the recommendations and all the other
20 Federal Government activities that are going on and
21 you know, we'll see what -- but we're not beholden to
22 the NAS study in any way but we certainly value their
23 view as a data point. As I said, there's many
24 projects going on, on alternative sources and they
25 have a very -- they came out with a very strong view

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1 on some things and those things need to be considered.

2 DR. VETTER: Just one other question. I
3 appreciate what you said about determining -- I
4 appreciate two things. One is that you came to us
5 even before that horse was out of the gate. It's
6 unusual. Usually we're trying to catch up with the
7 NRC but here you came to us early and we had an
8 opportunity for input very early. We appreciate that
9 very much.

10 The other is, we appreciate your interest
11 in the need to determine the impact and we hope that
12 we can help you sort through that. Do you know
13 whether Congress cares about that? And if so, how we
14 might --

15 MR. LEWIS: They've heard that certainly
16 from us at the congressional staff levels. I don't
17 know to the extent of where they've heard that from
18 other groups. They've heard, as well, from the NAS
19 panel itself. I think that as I said, before, what we
20 don't have is good data. We have antidotal stories a
21 lot on the impacts to the practice of medicine.

22 And frankly, you know, many doctors we've
23 talked to are in two camps; those that swear by x-ray
24 and those that swear by cesium chloride blood
25 irradiating. And so we hear it from both sides. I

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1 don't know that Congress has heard from both sides and
2 certainly any -- we are outreach. We're trying to
3 reach out to the industry, both the medical industry
4 and the source industry to make sure that they're
5 properly energized. The government, you know, will
6 have to take these recommendations and propose a path
7 forward to get it in front of people and get feedback
8 on the impacts.

9 CHAIRMAN MALMUD: Dr. Nag.

10 DR. NAG: I would like to reinforce the
11 statement that you made since I was on the
12 subcommittee. First of all, I'd like to thank all
13 that ACMUI members that allowed us to make the
14 comments on your behalf because there was only one day
15 to make that comment.

16 One is that the one thing is cesium
17 chloride. However, the public is likely to hear the
18 word cesium. Now, cesium, you can have cesium-131 and
19 cesium-137 and you can have the cesium-137 chloride in
20 the blood irradiator, which is quite different from
21 the cesium-137 used for low dose rate radiotherapy,
22 which is encapsulated. And my fear or the fear of the
23 subcommittee and hopefully the entire ACMUI, is that
24 the public will only hear cesium and therefore, will
25 view cesium-137 encapsulated and cesium-131 which is

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1 used for prostate implant as a new source in the same
2 light, and therefore, would try to eliminate those and
3 this is definitely not what the NAS wanted and not
4 what the ACMUI wants.

5 And I would like to reinforce that in any
6 statement that is made about cesium chloride.

7 MR. LEWIS: Yeah, I think that the NAS
8 recognized that they were talking about a unique
9 chemical and, in fact, we have the same concern there
10 as -- there's -- cesium, we don't know why they use
11 nuclide in any industrial or medical setting and many
12 of the smaller sources are not cesium chloride.
13 They're ceramic or vitrified form of cesium that don't
14 have the same disbursability issue or chemical
15 solubility issues that cesium chloride has and that's
16 a communication challenge we have to explain to people
17 why there's cesium chloride and then there's cesium in
18 two different topics.

19 MR. HUFFERT: If I could just build on
20 that. The report itself goes into some detail on that
21 but it's the recommendations which get the headlines,
22 which basically summarizes a very, I think,
23 inadequately. It should have said cesium-137 and not
24 cesium chloride.

25 MR. LIETO: That was going to be one of

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1 my --

2 CHAIRMAN MALMUD: Mr. Lieto.

3 MR. LIETO: Ralph Lieto. So the
4 recommendations really only refer to the salt forms of
5 cesium, not just cesium-137.

6 MR. HUFFERT: No, it's based on the form
7 of cesium and it's not only the medical industry that
8 could be impacted with that headline. It's also the
9 oil industry because they also use cesium but it's in
10 a different form. It's typically in a vitrified form.

11 DR. NAG: And that's what's recognized by
12 the -- when we went through it, but we also recognized
13 that the headline doesn't say it that way. So we --
14 I, at least, would like to make a recommendation that
15 whenever the cesium chloride be referred to in any
16 document, it be stated that this is cesium chloride,
17 as the salt and not cesium-137 that is ceramic based
18 and not other isotopes of cesium. So rather than just
19 saying cesium chloride and leaving the other thing
20 unstated, it has to be stated any time cesium chloride
21 is stated. That's a recommendation that we can make.

22 MR. LEWIS: I think the main impact is
23 blood irradiators and research irradiators, so as I
24 said there's 1100, I think. Essentially, almost all
25 of those are cesium chloride in a sealed source form.

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1 DR. NAG: And the other comment, I think,
2 that the subcommittee had was that the NAS has
3 mentioned the use of alternative sources, the use of
4 electrically or simulator-based sources, but has not
5 really dealt with adequately the impact of that, the
6 cost of that and also the effectiveness of that. Some
7 of these things can be a replacement, an alternative,
8 but may not be as effective and you know, that has not
9 been -- that is a strong recommendation that we would
10 like to make. Any other --

11 CHAIRMAN MALMUD: Dr. Fisher?

12 DR. FISHER: Yes, thank you for your
13 presentation. I'm curious on Recommendation 3, if you
14 might have any insights as to why the National
15 Academies emphasized replacing Category 1 and Category
16 2 sources as opposed to increasing the safety and
17 security of existing sources that are useful in
18 medical practice.

19 MR. HUFFERT: I think what they're trying
20 to do is they're trying to recommend to decrease the
21 overall inventory of cesium chloride in the United
22 States period. They have incentives pushing people
23 away from cesium chloride and pulling them towards an
24 alternative technology. Everything that they state in
25 I think it's Chapter 9 or 10 is really geared towards

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1 reducing the inventory of cesium chloride in the
2 United States and that's really what was their number
3 one goal of this report.

4 MR. LEWIS: They considered the security
5 measures, you know, between the time their study
6 started and the time their study ended the NRC
7 increased controls orders were issued which increased
8 security and implemented and the Agreement States
9 followed suit. And they talked some, I think, about
10 further increasing security but they're giving the,
11 you know, the lighthouse approach is at the end of the
12 day the cesium chloride should be replaced because
13 there's an alternative, it does exist.

14 We asked the same question of why
15 additional security measures couldn't be an
16 alternative to -- with the same effectiveness of
17 replacing the source all together.

18 MS. GILLEY: Debbie Gilley. In light of
19 wanting to do away with or replacements, do we have a
20 disposal option for cesium chloride in the 35 states
21 that don't have a compact? I'm going on the record of
22 bringing disposal up since that's going to be an
23 issue.

24 MR. LEWIS: Well, I think that they would
25 not be, insofar as they were greater than Class C low

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1 level waste, there would currently be no permanent
2 disposal option but the Academy would probably view
3 getting them in the hands of the government, whether
4 it be through DOE or somehow getting them out of the
5 hospitals and into a more secure place for temporary
6 storage pending disposal as some of the incentives to
7 push full incentives and I think we have to explore
8 that.

9 In fact the Energy Policy Act Task Force
10 has an effort to look at those kinds of issues. The
11 end of life of these sources is -- as much as that can
12 be better defined, it only improves, you know,
13 security of these sources if they have an ultimate
14 disposition, otherwise people have no reason to go
15 there.

16 MS. GILLEY: Thank you.

17 CHAIRMAN MALMUD: Dr. Thomadsen.

18 DR. THOMADSEN: Thomadsen. Depending on
19 what their fate is, if there's no place to put them
20 other than congregating them together in a given
21 location. That sounds like that might even be a
22 greater target for terrorists if you have all these
23 very large cesium chloride sources in one location,
24 regardless of how well secured, terrorists teams might
25 have a very great incentive to find those.

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1 MR. LEWIS: If it was a government-wide
2 solution, I think that the amount of material we're
3 talking about here is very small. It's big for us but
4 it's small in compared to the amount of sources that
5 DOE may already stored at some of their labs. You
6 know, Hanford or Savannah River have very large
7 inventory sources of plant fuel already, high level
8 waste. So I think that that's a good point that needs
9 to be considered when it's consolidated, but I think
10 as I said, it's a government-wide solution and looking
11 at the totality of the issue that these will be
12 dwarfed in the tidal wave of other sources that exist.

13 MR. HUFFERT: And one thing that the
14 report did say is they were concerned about these
15 sources going overseas to a less secure environment.
16 They are interested in making sure that the sources
17 remain in a secure environment and perhaps the U.S.
18 would be a better alternative than them going abroad.

19 CHAIRMAN MALMUD: Dr. Welsh.

20 DR. WELSH: I have a question about the
21 statement that alternatives exist for cesium-137 at
22 this point and these questions might reflect my
23 ignorance on the subject as a whole but I understand
24 that cesium-137 has been the standard in medical
25 practice for blood irradiators. It has a 662 keV

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1 gamma. It's got a long half life but we can be
2 comfortable with our clinical experience with the
3 energy and the dose rate.

4 Has there been a direct comparison between
5 the electronically generated irradiators, radiation
6 sources versus the cesium, so that we can be confident
7 that this is a true equivalent? I know Dr. Nag
8 brought this up but has there been -- is there
9 evidence that this is equivalent, there is an
10 equivalent out there?

11 MR. LEWIS: I think there has been some
12 research in the literature on that topic and it boils
13 down to how well filtered the x-ray would be. If the
14 x-ray is sufficiently filtered, it will have a dose
15 distribution across the blood bag that's a little more
16 tilted than a mono-energetic cesium would be but at
17 the end of the day as long as you use the blood right
18 away in the patient and you give the entire blood, 25
19 Gray, I think is the target dose, then it's equally
20 effective.

21 Costs, in administrative costs, I'm pretty
22 sure x-rays is rather higher, I've heard double. But
23 in terms of the technologically effectiveness,
24 technical effectiveness, I think the studies have
25 shown that either one can be used. I think that

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1 that's for blood irradiation. I think that the same
2 end use may be a little more tricky for research.

3 If you're irradiating an animal and the
4 physics of the scattering is such that there will be
5 preferential energy deposition around the bone, you
6 may be trying to kill the marrow and that's exactly
7 where you want to have a very repeatable experiment
8 for your research and causes some trickier questions.

9 There is a vendor that sells both and I
10 talked to that vendor and they told me that there's
11 pros and cons of both and as I said before, I think
12 some physicians swear by x-ray and some seem to swear
13 by cesium and what we need help on is getting more
14 than antidotal information, but systematic
15 information.

16 MR. HUFFERT: The one person that was on
17 the National Academies Study Committee was from the
18 American Red Cross and he is in charge of the blood
19 department there, the research and development part of
20 it. And I asked him that very question, which you
21 asked was, are these alternatives effective? And his
22 position was that yes, they are effective.

23 Now, on the alternative technology sub-
24 group of the task force, we asked this question to
25 representatives of the NIH and one of the people said,

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1 no, that they're quite happy with cesium and they
2 aren't willing right now to make that switch. So we
3 have antidotal evidence, but I think the position of
4 the National Academies was that they are effective.

5 CHAIRMAN MALMUD: So if I understand your
6 presentation, the purpose of it is to solicit from the
7 Committee advice from persons on the Committee how are
8 intimately involved with cesium and its applications
9 certainly in blood irradiation and perhaps, in
10 research as well. You don't have to look very far to
11 find somebody who is intimately involved in this.
12 Would you be willing to serve as a consultant to Rob
13 and Tony on this issue?

14 DR. VETTER: Sure. When are you looking
15 for information?

16 MR. LEWIS: As we move forward, like I
17 think our mentioned, our primary vehicle to advance
18 these issues is going to be the Energy Policy Task
19 Force subgroup on cesium and they owe a product, I
20 believe in the August time frame. They certainly will
21 be developing that product sooner than that and in
22 fact, engaging the industry in May/June time frame and
23 at that point, I think, if you'd be willing, we would
24 seek out advice from the Committee.

25 CHAIRMAN MALMUD: Dr. Vetter is one. Who

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1 else on the Committee is involved with the use of
2 cesium regularly in both research and in blood
3 irradiation. We have two more, Dr. Fisher and Dr.
4 Thomadsen. I'm sorry, and Ralph.

5 MR. LIETO: I've got experience with both
6 systems.

7 CHAIRMAN MALMUD: You do.

8 MR. LIETO: And I've got some comments. I
9 didn't know if we were going to be presenting these
10 after Dr. Nag and Dr. Vetter's presentation or they
11 wanted to solicit them now or do you want to wait till
12 they get to that point, or where we're going.

13 CHAIRMAN MALMUD: I'm looking for some
14 names now and then the discussion would follow. So it
15 appears that there are four members of this Committee
16 who have that knowledge base that you might be seeking
17 and they are Dr. Vetter, Dr. Thomadsen, Dr. Fisher and
18 Mr. Lieto. Did I miss anyone else who has got the
19 experience? Is four a good number for you, too many,
20 too few?

21 MR. HUFFERT: It's excellent.

22 CHAIRMAN MALMUD: And you'll get diverse
23 opinions, I guarantee you from among these four
24 gentlemen, but they'll be valid opinions. Do you all
25 agree? Do you have the time and willingness to

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1 commit? Ralph? Okay, you have the four individuals.

2 MR. LEWIS: Thank you. That's all the
3 comments I had, unless there's any more questions for
4 me.

5 CHAIRMAN MALMUD: We achieved your goal,
6 Tony, Bob. Okay, thank you. We'll move back to our
7 agenda if we may. And the next item on the agenda is
8 the report of the NAS report briefing.

9 DR. NAG: I think basically, you would
10 want the report of the NAS, so I ask the Board, I
11 wonder, I think it would be a waste of time to add
12 anything further because all of the things we have
13 already discussed in this report.

14 CHAIRMAN MALMUD: Thank you, and it's in
15 the report which is Agenda Item 4 in your folder, in
16 your book and it was updated with material that was
17 distributed this morning as well. If you did not have
18 that, it's available here.

19 Thank you. Then we'll move onto Item
20 Number 5 which is the Elekta Perfexion. And that is -
21 - oh, I'm sorry, Mr. Lieto?

22 MR. LIETO: I just had a quick question.
23 Is the full report available, because we've got
24 summaries and links to summaries and those types of
25 things but I don't think the links that we have are to

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1 the actual report or is that sort of still classified?

2 MS. TULL: This is Ashley. I sent you
3 guys a copy. It's a link to the NAS site. It's the
4 full report and I actually have a binder with three
5 copies if you guys want to look at these or take these
6 over here. You have to kind of log in with your e-
7 mail address to get that link to work.

8 MR. LIETO: Okay.

9 MR. HUFFERT: And we're getting hard
10 copies of the final report very soon.

11 MS. TULL: If you guys want to see
12 anything today, though, I have copies down here.

13 CHAIRMAN MALMUD: Thank you. Dr. Nag,
14 you're on.

15 DR. NAG: There was a subcommittee review
16 with the Perfexion model of the gamma knife. The
17 problem was the when 35.600 was written, there was no
18 Perfexion. There was only the Elekta gamma knife
19 which did not have -- which has trunnions and helmets.
20 The new gamma knife does not have some of these
21 components. And therefore, the new Perfexion gamma
22 knife cannot fulfill those conditions.

23 And therefore, the new Perfexion gamma
24 knife had to be placed under 35.1000 as a new
25 modality. At the last ACMUI meeting, it was

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1 recommended that the 35.600 be modified such that it
2 will be -- enable the Perfexion to fulfill the
3 requirements. The subcommittee will -- Dr. Thomadsen,
4 Dr. Welsh, Mr. Lieto and Ms. Gilley and we had
5 requested three other people who have experience with
6 the Perfexion to aid as consultants and they were Dr.
7 Aqualino, Dr. Goetsch and Dr. Suh.

8 Especially Dr. Aqualino, who is at the
9 University of Pittsburgh and has used this a lot, has
10 helped us very much in providing many of the wordings.

11 So basically, if you will see the handout under
12 Section 5, we have made just some minor modifications
13 whereby we have used wordings that are -- instead of
14 having the word helmet there, we have a more
15 generalized wording such that not only the new gamma
16 knife, the Perfexion model, but also the Chinese gamma
17 knife that is coming out or that is out will also be
18 able to fulfill it, so we have made all the wording
19 very generic instead of being specific to the Elekta
20 gamma knife.

21 I will not go through each and every word
22 but basically on page 1, what we did is that we made
23 it applicable to all models, so you can see how we
24 deleted just the word. And for example, on page 2, we
25 just put the word collimator output and collimator

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1 system rather than putting trunnions and helmets. So
2 this way it would be more generic and all
3 encompassing, and throughout the entire document, we
4 just changed the words so that it would be all
5 encompassing. So if you have any questions on any of
6 them, basically it's just changing the wording of
7 helmet and trunnions and replacing them with more
8 generic words and that was all that was needed and we
9 felt that having it more generic would allow at least
10 most of -- all the current forms of gamma knives now
11 and hopefully many of the future gamma knives to be
12 able to accommodate this 35.600.

13 I think I'll leave it at that and ask for
14 any questions. All of them we have indicated where we
15 changed the word, so it should be very clear to all of
16 you.

17 CHAIRMAN MALMUD: Thank you, Dr. Nag. Are
18 there questions for Dr. Nag? We'll give the members
19 of the Committee just a few more minutes just to go
20 through this.

21 DR. WELSH: I have a simple question for
22 Dr. Nag.

23 CHAIRMAN MALMUD: Dr. Welsh.

24 DR. WELSH: What is the name of the
25 Chinese unit? Is that OUR/American?

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1 DR. NAG: I don't know. I mean, that was
2 something that one of the physicist consultants
3 brought up that the Chinese version and I think Bruce
4 might know.

5 DR. THOMADSEN: I don't remember. They
6 came and gave a presentation to us, but I don't
7 remember now.

8 CHAIRMAN MALMUD: Other questions? Thank
9 you.

10 DR. NAG: As I had mentioned, I thought
11 that this would take a very short time and that's why
12 I would have a few minutes. What I would like to ask
13 the ACMUI is that there was a -- there was a 35 draft
14 language for permanent brachytherapy that was sent to
15 all of your on and not for public knowledge on
16 February 21st, 2008. That document went through some
17 of the wordings that would be subject to rulemaking
18 for permanent brachytherapy and this would be under 10
19 CFR 35.40 and 35.3045. If you don't have the detail
20 with you now, I won't go into detail, but what I would
21 like is to request that the ACMUI have a separate
22 teleconference to discuss this because I feel that
23 some of the wording may be problematic and I would
24 like to have the full ACMUI members discuss that and
25 if possible, to have in that discussion one or two

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1 more consultants who do brachytherapy to give a more
2 representative view. So that is a motion that I would
3 like to make.

4 CHAIRMAN MALMUD: Dr. Nag is making a
5 motion for what amounts to a conference call which
6 would be among the members of the Committee and also
7 asking for permission to invite one or two consultants
8 who are not members of the Committee but who are
9 knowledgeable in the area to join that committee
10 meeting, which would be a conference call. This would
11 be not a conference call for the public; is that
12 correct? That's a motion. Dr. Welsh --

13 DR. WELSH: I second.

14 CHAIRMAN MALMUD: -- seconds the motion.
15 Is there discussion of the motion or are there
16 concerns from the NRC staff regarding the
17 appropriateness of this?

18 DR. NAG: Just quickly, having a member
19 who is not a member of the ACMUI but a consulting
20 member in a conference call, would that be
21 problematic.

22 MS. TULL: This is Ashley. As long as
23 you're doing subcommittee work, it's fine.

24 CHAIRMAN MALMUD: Thank you, Ashley. Dr.
25 Vetter, you have a comment?

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1 DR. VETTER: Could somebody just clarify
2 again the purpose of the meeting?

3 DR. NAG: In February, the NRC released a
4 preliminary draft that would change some of the ruling
5 for permanent brachytherapy. And you know, in it some
6 of the wording included that if it shows more than
7 three centimeters away and you know, if that more that
8 show in the periphery and point that would be
9 constituting a medical event. So some of these things
10 came from original discussion at ACMUI, I believe two
11 years ago. And some of them may have been -- some of
12 the ACMUI discussion may have been misinterpreted when
13 the rulemaking came into play and therefore, we would
14 like that discussed at an AMCUI before the rule moves
15 forward.

16 DR. VETTER: And what's the time line on
17 the rule?

18 DR. NAG: I believe that in February they
19 had sent an initial draft out for comment and then
20 they are -- if Ed Lohr is here, he might be able to
21 give us -- but some time in this summer, I believe,
22 they are going to resend it out for public comments.

23 CHAIRMAN MALMUD: Mr. Lieto?

24 MR. LIETO: Yeah, I know what Dr. Nag is
25 referring to but I'm just wondering, it might be a

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1 little bit premature here. Maybe, because I know that
2 people commented on it, I know I did and others and I
3 think it was sent out to Cindy. I think maybe what we
4 ought to do is see how they incorporate all the
5 comments, sort of as an advanced publication to
6 rulemaking or something like that to see how they're
7 taking the comments and suggestions.

8 DR. NAG: That came out last week.

9 MR. LIETO: Oh, okay, well, I didn't know
10 that it came out last week.

11 MS. FLANNERY: And that's -- if I can talk
12 here, and that's the reason why we can't talk about it
13 here at this meeting is because that document was sent
14 to you, ACMUI as a pre-decisional document. So we
15 would have to defer it to a teleconference at a later
16 time and keep it closed.

17 MR. LIETO: All right.

18 DR. NAG: And that is why I'm not bringing
19 it up for discussion at this meeting and I would like
20 a closed teleconference and I think it will be more
21 effective if we had a couple of other members who are
22 experienced and knowledgeable in permanent
23 brachytherapy.

24 CHAIRMAN MALMUD: Cindy?

25 MS. FLANNERY: A couple of things. You

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1 were asking about having members of the public
2 participate in a closed session.

3 DR. NAG: Consultants.

4 MS. FLANNERY: Consultants.

5 DR. NAG: People who have done a large
6 number of implants. I have done a large number of
7 implants but, you know, other people who, you know,
8 may --

9 MS. FLANNERY: You're talking about non-
10 special government employees, correct?

11 DR. NAG: Non-government employees but who
12 are specialists in permanent brachytherapy.

13 MS. FLANNERY: I need to look into that
14 because I don't know the answer to that.

15 DR. NAG: But at least I would definitely
16 like if there is going to be a subcommittee meeting, I
17 would definitely like people who are involved in
18 permanent brachytherapy from the Committee to be on
19 that subcommittee and if possible an additional one or
20 two members but if that --

21 MS. FLANNERY: This isn't a full committee
22 meeting. You're talking just a subcommittee.

23 DR. NAG: Whatever would work.

24 MS. TULL: That's what I was trying to
25 explain a second ago. If you do a subcommittee

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1 meeting, there is no issue on it being closed to the
2 public and you can consult with others. I don't know
3 about actually having them on the call but as far as
4 sending them an e-mail and asking for their comments,
5 incorporating that into your subcommittee discussion,
6 we can close off a subcommittee meeting. I can set up
7 a teleconference.

8 If you want to do a full committee
9 meeting, we've got to go talk to Office of General
10 Counsel and find out whether or not we can close the
11 meeting.

12 DR. NAG: In that case, I think our
13 purpose would be served by having a subcommittee
14 meeting that would include a radiation oncologist and
15 a radiation physicist at the minimum and anyone else
16 who would want to be on that subcommittee, plus at
17 least one or two other consultant members. That would
18 be a subcommittee meeting. It would be a closed
19 subcommittee meeting.

20 MS. FLANNERY: Is the purpose to bring
21 your concerns to NRC staff?

22 DR. NAG: The purpose would be to bring my
23 concern as well as the concern of others who do a lot
24 of permanent brachytherapy because if you're not doing
25 a lot of permanent brachytherapy, you may or may not

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1 know all the implications of the wording of people who
2 attend. So, I mean you have someone who's never done
3 permanent brachytherapy to be in that committee would
4 not really add much, but someone who's done a lot and
5 sees some of the indications would really be
6 meaningful. So I want to have some meaningful input
7 and not just mine.

8 It may be my concern but, you know, if
9 four other people who are doing 1,000 implants like
10 me, do not have that concern, then I'm willing to
11 withdraw my concern.

12 MS. FLANNERY: And the reason I'm asking
13 these questions is depending on what type of meeting
14 that we have and what the purposes will determine,
15 whether this is just a subcommittee meeting, which
16 does not need to be announced in the Federal Register
17 beforehand.

18 If it is a public meeting, whether it -- I
19 should say if it is a full committee meeting, whether
20 it's public or whether it's closed, it has to be
21 announced. And we're talking about a month out. And
22 if the purpose is to, you know, bring the concerns and
23 recommendations to NRC, that really should be a full
24 committee. And you can meet as a subcommittee before
25 then to get everything together to prepare for that

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1 full committee meeting, but a full committee meeting,
2 whether it's closed or open, has to be announced, but
3 we can certainly arrange that if that's what you want
4 to do.

5 DR. NAG: I would like the advice of the
6 Chair. Do you think this should be -- you are aware
7 about what we are going to discuss. Is it better
8 served in a committee or a subcommittee meeting?

9 CHAIRMAN MALMUD: I think it might be best
10 to do a full committee which would be a public
11 announcement.

12 DR. NAG: One thing, if it's a public we
13 cannot discuss the second --

14 MS. TULL: No, Dr. Nag is correct as well.
15 You would not be able to discuss pre-decisional
16 information in that public meeting.

17 DR. NAG: Right.

18 MS. TULL: We would have to get OGC to
19 approve a closed meeting then the public would not be
20 participating and you would not be able to have
21 consultants or outside -- someone who's not a special
22 government employee.

23 DR. NAG: So I think we would be better
24 served in a closed meeting.

25 CHAIRMAN MALMUD: You would prefer a

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1 closed committee.

2 DR. NAG: Closed subcommittee meeting and
3 then if we need to have a -- by that time, it may be
4 that we would be able to put it on the agenda for the
5 next full ACMUI meeting in October.

6 CHAIRMAN MALMUD: The way my thinking was
7 going when I began to answer your question was that
8 might there be concern from other members of the
9 radiation oncology community as to why only several
10 individuals who are not on the Committee were
11 solicited for their opinion when other radiation
12 oncologists may have very strong opinions that
13 wouldn't have been represented, because a subcommittee
14 meeting is neither open to the public nor is it a
15 closed meeting in which we are discussing things
16 amongst ourselves. So that's what my concern was in
17 addressing it. But if you feel that that's not the
18 case, I'm perfectly flexible. Rob?

19 MR. LEWIS: Let me suggest a third
20 confusing alternative. In the past, when we have a
21 difficult rulemaking issue, we have issued as part of
22 a meeting announcement, a discussion draft which
23 describes an issue that people can come to the meeting
24 fully aware of the options and the issue without
25 actually getting into, you know, marking up draft rule

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1 text. And in those circumstances, the issue can be
2 fully described as part of the meeting materials in a
3 public way and that may be a path that the Committee
4 could pursue. It's your discretion but I just wanted
5 to make sure that was on the table.

6 CHAIRMAN MALMUD: Subir, does that
7 suggestion appeal to you or did you not hear it?

8 DR. NAG: Not fully.

9 CHAIRMAN MALMUD: Rob, would you just
10 repeat your suggestion?

11 MR. LEWIS: Another alternative where the
12 meeting could still be a public meeting is as part of
13 the meeting materials, a draft issue paper or a white
14 paper or whatever you call it, can be developed as
15 part of the public meeting materials that everybody
16 can have and everybody can talk about. And it gets to
17 the heart of the issue. But the ground rules in those
18 cases, you can't have the draft rule text and have
19 people marking up the draft rule text before the
20 proposed rule is out.

21 I would -- yeah.

22 DR. NAG: The draft that was sent out in
23 February of 21, was a public document and we can have
24 our discussion based on that public document of
25 February 21st, which everyone has and the public has.

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1 And for the concerns that we have, that is all that
2 is required to address some of the concerns.

3 CHAIRMAN MALMUD: So that, therefore, if I
4 understood you correctly, you are proposing to have a
5 subcommittee meeting referencing the document which
6 was a public document and not the detailed background
7 material which was not public.

8 DR. NAG: Right, and that would allow us
9 to have consultants. That would allow us to have
10 input and then, you know, if we need to discuss
11 anything else, that can be a separate issue.

12 CHAIRMAN MALMUD: So the consultants could
13 be brought in as long as you don't cross the line
14 between the public document and the background
15 material.

16 DR. NAG: Right.

17 CHAIRMAN MALMUD: And that's your motion.

18 DR. NAG: Right.

19 CHAIRMAN MALMUD: Is there a second to
20 that motion?

21 DR. THOMADSEN: I'll second it.

22 CHAIRMAN MALMUD: Dr. Thomadsen seconds
23 it. Now, is there discussion of the motion and its
24 purpose? Mr. Lieto?

25 MR. LIETO: Yes. In order for him to

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1 voice the concerns with the proposed rule, I mean, it
2 was my understanding it was the implementation in the
3 proposed rule that's raised the concerns.

4 DR. NAG: No, my concern was about the
5 draft that came out in February of '08. That, I
6 really had concerns about that. Now, this happened --
7 this is a further modification of that, which we are
8 not going to decide but even this last February 21st,
9 is still -- you know, it still needs to be discussed.

10 MR. LIETO: Let me rephrase it then, the
11 issue is then the February -- not ours but preliminary
12 draft ruling which was sent to everybody and also was
13 published and people have commented on that and those
14 comments have been, I take it, in process.

15 MS. FLANNERY: That's correct.

16 MR. LIETO: How do we not know that staff
17 hasn't implemented your concerns in that already? I
18 mean, I guess I'm trying to understand, what is the
19 problem we're trying to solve if staff is still
20 getting their arms around all the comments that have
21 come in and we haven't seen the results of those
22 comments? Your problems or your issues may have been
23 addressed.

24 MS. FLANNERY: Correct me if I'm wrong,
25 but you were just sent a pre-decisional document

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1 recently, within the last couple weeks, I believe, and
2 that would have incorporated your comments to the
3 preliminary open document, preliminary draft language;
4 is that correct, Ron?

5 DR. NAG: Which is not public.

6 MS. FLANNERY: Oh, it's not public.

7 MR. LIETO: I think we're dealing in the
8 abstract of your concerns not knowing what the
9 specifics of those concerns are. And you want to have
10 the subcommittee or full committee meeting, but what
11 are the specifics of the concerns that you want to
12 address? I mean --

13 DR. NAG: I'm ready to address that in
14 that subcommittee meeting. And, you know, you are
15 saying how do you know that they haven't been
16 incorporated? I know it because of this which is not
17 released to the public.

18 MR. LIETO: But we don't want to discuss
19 that document.

20 DR. NAG: Right, we don't, so I want to
21 still discuss the original document. The original
22 document is still open for discussion.

23 CHAIRMAN MALMUD: Dr. Vetter?

24 MR. LIETO: I don't see the need for a
25 subcommittee meeting at this time because I think what

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1 we need to do is get Dr. Nag's specific concerns with
2 this document that was just released as pre-decisional
3 to the Committee, all right, and maybe go from there.

4 Maybe the concerns don't require a committee meeting.

5 I mean --

6 CHAIRMAN MALMUD: Dr. Vetter?

7 DR. VETTER: Yeah, this is Dick Vetter.
8 If this is the same subcommittee that we've been
9 talking about before, aren't subcommittees authorized
10 to simply work with staff to schedule a meeting?

11 MS. TULL: Yes.

12 DR. VETTER: Then we don't need the full
13 Committee's involvement in -- if he wants a
14 subcommittee meeting, he just talks to the staff about
15 having a subcommittee meeting.

16 DR. NAG: Wait, this is not a
17 subcommittee. This is --

18 DR. VETTER: Oh, you're talking about a
19 new subcommittee.

20 DR. NAG: This is the one on permanent
21 brachytherapy. This is not --

22 CHAIRMAN MALMUD: Sally.

23 MS. SCHWARZ: I have a question in regard
24 to the possibility of just discussing this at this
25 meeting. Will there be a portion of the meeting that

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1 will be closed that this document could be discussed
2 within the next two days and then from that point, you
3 can make your --

4 DR. NAG: Yeah, I had asked for that.
5 There was no time between today and tomorrow to have a
6 full discussion which is why, I mean, the suggestion
7 was brought up that we have a separate either
8 subcommittee meeting or a separate committee meeting.

9 MS. TULL: Cindy, this is Ashley. I have
10 a question. We do have a closed session this
11 afternoon. Can't we, at the discretion of the Chair,
12 if you want to stay after your Commission presentation
13 discussion stay and discuss this topic? We will be in
14 a closed session. I believe that's Dr. Malmud's
15 decision to add an agenda topic, however late you want
16 to stay.

17 MS. FLANNERY: The closed session is
18 scheduled until 5:30.

19 CHAIRMAN MALMUD: We have the Commission
20 briefing preparation, which is scheduled until 5:30.
21 And therefore, I was not certain that there was any
22 time available to do this today. I had not personal
23 objection to it, but it seems that today's agenda is
24 rather full. Do you want to extend it beyond 5:30:
25 Is that it?

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1 DR. NAG: I think it would be best if we
2 have a separate subcommittee meeting, a small
3 subcommittee. Those of you who want to be on the
4 subcommittee, in addition to the radiation
5 oncologists, are welcome to be on there. And, you
6 know, that will have the full implication because when
7 you get some of the comments back and so forth, you
8 don't have a full discussion on some of the
9 implications. Some people can comment back and so
10 forth but not the full discussion.

11 And the reason I do not want to wait until
12 the next Committee meeting for that discussion, is by
13 then many of -- it's like a running plane, if the
14 plane is going full speed, and you don't have a
15 mechanism to -- you don't want to stop it in the
16 middle of track but you want to provide input, you
17 need to provide meaningful input beforehand.

18 CHAIRMAN MALMUD: Thank you. You've made
19 a motion, it was seconded and now Dr. Zelac has a
20 comment.

21 DR. ZELAC: Just a few things that might
22 help in resolution of this issue. First is, that the
23 proposed rule which you have seen a pre-decisional
24 copy of, is working through the concurrence chain now
25 and the intent is to, of course, have that published

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1 as soon as possible which is likely to be in very
2 early June.

3 So at that point, the document becomes
4 public and it's available for comment from everyone
5 who would have opportunity to see it and interest in
6 it, including the Advisory Committee, individual
7 members of the Advisory Committee, whatever. Any
8 input with respect to what it is at this point is
9 probably not going to have any impact on the proposed
10 rule itself. In fact, I could almost say with
11 assurity from my level that the proposed rule is going
12 to go out as it is now for comment.

13 You've had an opportunity to see it, to
14 have additional time to mull it over and think about
15 it but I don't believe that it's in anyone's best
16 interest that we try to now modify what's already
17 scheduled to be published as soon as possible based on
18 further input from the Committee at this point in
19 time.

20 CHAIRMAN MALMUD: Thank you, Dr. Zelac.
21 Did you wish to reply, Dr. Nag?

22 DR. NAG: In that case, what we could do
23 is have a full committee meeting before the fall
24 meeting but after the publication of this public
25 draft, so that we can discuss some of the

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1 implications. None of these are going to be changed
2 between now and the publication of that draft.

3 CHAIRMAN MALMUD: So your recommendation
4 at this point is that we await the publication of the
5 document for the public at which point comments are
6 invited from all parties, including this Committee
7 itself and make -- and have a conference call at that
8 point regarding the issues.

9 DR. NAG: My -- the problem is that by the
10 time it's published and then the whole Committee tries
11 to get together and form a meeting, it takes -- you
12 know, you have to have a two-week notification. You
13 have to get these things going. We may not have
14 sufficient time. That was the reason for us trying to
15 have a closed committee meeting so we knew what are
16 the things that are problems and then once it becomes
17 public, we can then make a public announcement of
18 public meeting.

19 CHAIRMAN MALMUD: I understand. So is
20 your motion still on the floor unchanged?

21 DR. NAG: Yeah, my motion is that we have
22 the subcommittee meeting separate. We -- you know,
23 that we know it's not going to be acted upon but the
24 moment it becomes public, then we can, you know, send
25 the subcommittee report out if needed to the whole

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1 Committee.

2 CHAIRMAN MALMUD: And that's your
3 preference above waiting for it to be public and then
4 having a subcommittee or a committee, either one, via
5 telephone to respond to it.

6 DR. NAG: Right, so that at least we know
7 what the problems are. Since we know, you know, not
8 even the wording but what the -- what the concerns
9 are, we know what the concerns are.

10 CHAIRMAN MALMUD: Mr. Lieto, you had your
11 hand up.

12 MR. LIETO: No, just rubbing my temples.

13 CHAIRMAN MALMUD: So there's a motion
14 that's been moved -- I'm sorry, Dr. Zelac.

15 DR. ZELAC: Two comments, which again, may
16 have some relevance here. First, once the proposed
17 rule is published, the comment period, the period
18 during which comments are invited is 75 days long. So
19 that's the first thing.

20 Second thing is that the proposed rule,
21 which will be going out reflects as best as we and
22 staff have been able to do, the input, the specific
23 recommendations of the Advisory Committee, which were,
24 of course, based on the input and recommendations of a
25 subcommittee. So we have tried on staff level to look

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1 at the advice from the Advisory Committee and
2 incorporate that into appropriate rule language which
3 you have had an opportunity to see in terms of what
4 the recommendations would be, what the input would be.

5 But my point is that this is certainly not new and we
6 may be talking about some small adjustments but the
7 basis for what's in the proposed rule reflects the
8 input that we got from the Advisory Committee.

9 CHAIRMAN MALMUD: Dr. Nag?

10 DR. NAG: Yeah, and I'm fully aware about
11 that, and I'm fully aware that many of that input of
12 that subcommittee were from me and my main concern was
13 that some of those have been taken out of context when
14 the rule was finally being made and that is the reason
15 why I want this subcommittee meeting in the first
16 place. But I do not want in six months from now what
17 is to become the rule and then be said, "Well, you
18 were the one who had provided this input in the first
19 place." I think that is a major problem and that is
20 why I want to have this discussed.

21 CHAIRMAN MALMUD: And you don't believe
22 that this will be achievable in the 75-day comment
23 period after the document is released?

24 DR. NAG: If everything goes on time and
25 we are aware on the first day and then we immediately

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1 ask for the sub -- a committee meeting, maybe it's
2 possible but I am somewhat -- you know, like many of
3 these things, the ACMUI members are not aware that
4 this one was circulated. You know, we get so many e-
5 mails that some of these things we may not even know,
6 you know, are out.

7 Like this e-mail was sent out what about
8 two weeks ago. Half the Committee members don't know
9 that this e-mail was sent out to us. The other one in
10 February was sent out but not everyone goes through
11 line by line to know what the problem could be.

12 CHAIRMAN MALMUD: Thank you. So there is
13 a motion on the floor. Any further discussion of the
14 motion? All in --

15 DR. THOMADSEN: Could you repeat the
16 motion, please?

17 CHAIRMAN MALMUD: Dr. Nag's motion is that
18 there be a subcommittee meeting scheduled to discuss
19 the elements of the document that are discussable with
20 a consultant.

21 DR. NAG: If possible --

22 CHAIRMAN MALMUD: If possible.

23 DR. NAG: -- with a consultant also, but
24 at the --

25 CHAIRMAN MALMUD: Addressing only the

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1 issues that were made public and not -- obviously, not
2 addressing the issues that are not yet public. That's
3 Dr. Nag's recommendation. The concern is that this
4 may be -- the other opinions we're hearing are in
5 opposition to this because the concern is that a
6 complete discussion will not be able to occur because
7 the details are not yet public and therefore, cannot
8 be brought into the discussion, and that there will be
9 an opportunity which is a 75-day period following the
10 publication of the draft document.

11 So it's simply a question of going for
12 this Committee meeting or not and Dr. Nag's motion is
13 to go for it.

14 DR. THOMADSEN: One question; if we were
15 to have the entire Committee discussing it and have
16 notice put out, how far ahead does that have to be?

17 CHAIRMAN MALMUD: Two weeks.

18 MS. TULL: This is Ashley. It's about a
19 month to get the whole thing put together. By the
20 time I e-mail everyone, we come to a consensus, and
21 then put the Federal Register notice together and then
22 it take another three days for them to publish it.

23 DR. THOMADSEN: So of the 75 days, if we
24 wait until that comes out, and we and to have the
25 Committee discuss it --

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1 MS. TULL: Thirty.

2 DR. THOMADSEN: -- we take 30 of those
3 days just waiting before the Committee could meet.

4 DR. NAG: And it takes more than that
5 because many times, when you put out the notice, we
6 are not available, you know, yet even a subcommittee
7 meeting going takes a little longer. That's a minimum
8 I agree but --

9 MS. TULL: Well, let me clarify. For a
10 full committee meeting, a Federal Register notice is
11 required. For a subcommittee meeting, I can do what
12 I've always done. I'll call the NRC operator, set up
13 a bridge line. Four, six, 10 of you call in and you
14 do your own thing. I don't put that in the Federal
15 Register.

16 DR. THOMADSEN: No, I was asking for the
17 full committee question.

18 MS. TULL: Full, yeah.

19 DR. THOMADSEN: I just wanted information
20 on that.

21 CHAIRMAN MALMUD: Any further -- Dr.
22 Vetter?

23 DR. VETTER: I do have a little bit of a
24 concern about not having this noticed in such a way
25 that stakeholders as a whole could see what's going on

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1 here and have an opportunity for input. Secondly,
2 if it's a subcommittee, I think the charge has to be
3 extremely specific and I haven't heard a charge yet.
4 So I think we're getting the cart before the horse
5 scheduling a subcommittee meeting when we don't know
6 exactly -- I don't, I'm still confused about exactly
7 what the charge would be and who would be on the
8 subcommittee. So those two things bother me a little
9 bit about the motion.

10 CHAIRMAN MALMUD: Thank you. Anyone want
11 to call the motion?

12 DR. NAG: To answer your question, I think
13 the charge would be to discuss the Part 35 on
14 permanent brachytherapy, the proposed ruling on the
15 permanent brachytherapy and that was already made
16 public on February 21st and the subcommittee member
17 would be any member of the ACMUI but at the very
18 least, the ones who are involved in permanent
19 brachytherapy and that would be myself, Jim Welsh and
20 Bruce Thomadsen and anyone else who have knowledge of
21 permanent brachytherapy should be included.

22 I mean, I know these three -- the three of
23 us are included. If you involve yourself, that's
24 fine, but at the very least these three.

25 CHAIRMAN MALMUD: Care to call the

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1 question? All in favor of the motion? Three.
2 Opposed? Four. Abstentions.

3 MS. GILLEY: I can't vote yet.

4 CHAIRMAN MALMUD: So it's defeated. It's
5 four to three in opposition --

6 DR. NAG: That's fine.

7 CHAIRMAN MALMUD: -- with two abstentions.
8 In that case, we will expect --

9 DR. VETTER: Dr. Howe has a comment.

10 CHAIRMAN MALMUD: Oh, I'm sorry, Dr. Howe.

11 DR. HOWE: And this is only if you are
12 going to move back to the original topic of this
13 presentation. If you're still talking about the
14 public meetings, I'll defer.

15 CHAIRMAN MALMUD: You're asking if we're
16 going back to the presentation?

17 DR. HOWE: Yes.

18 CHAIRMAN MALMUD: Whether we're done with
19 this issue? I was just going to put a closing comment
20 on this issue and that is that we will await the
21 release of the document, recognizing there's a 75-day
22 comment period and if you contact us, either me, as
23 Chairman or staff here, requesting a conference call
24 for the topic, it will be arranged? Is that --

25 DR. NAG: Sure, that's fine with me. Can

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1 I request Ashley or whoever in the NRC staff to
2 specifically remind when the request comes. Sometimes
3 you know, we don't always, you know, see it in bold,
4 to let us know that this was -- this is coming out on
5 this and this date.

6 MS. TULL: Dr. Malmud, this is Ashley. If
7 anyone wants a copy of the pre-decisional document
8 that was sent out, I went and looked it up on the e-
9 mail. Everyone got it on April 22nd. And it was a
10 "for information only" document. So it's a copy of
11 the Federal Register notice that I can give you if
12 you'd like to look at it. That would be what would be
13 published later this summer.

14 CHAIRMAN MALMUD: Ashley, would it be
15 possible for you to send Dr. Nag an e-mail
16 specifically addressed to him on the date that this
17 document is released to alert him to it?

18 MS. TULL: Sure.

19 CHAIRMAN MALMUD: Thank you.

20 DR. NAG: In fact, what you could do is at
21 that point, you know, get the ball rolling on
22 arranging the teleconference.

23 CHAIRMAN MALMUD: She'll send you an e-
24 mail and then you can contact her regarding what you
25 see is necessary at that point. Do you have another

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1 comment, Dr. Zelac?

2 DR. ZELAC: Just a suggestion, since
3 you're all assembled now, it might be prudent and
4 worthwhile from a time point of view, to try to set up
5 a meeting now.

6 CHAIRMAN MALMUD: But do we know the date
7 of release yet?

8 DR. ZELAC: No, you don't but if you
9 scheduled your meeting for some time you know, in
10 July, you certainly should be fine, particularly if it
11 was near the end of July.

12 CHAIRMAN MALMUD: If you expect that the
13 document be released before July, that's fine.

14 DR. ZELAC: As I said, I think the
15 expectation at the moment is it will be early June.

16 CHAIRMAN MALMUD: All right.

17 DR. NAG: That's fine with me.

18 CHAIRMAN MALMUD: Can we do such a -- can
19 we set up a tentative meeting?

20 MS. TULL: Sure. Do you want a full
21 committee meeting, public?

22 CHAIRMAN MALMUD: Yeah, all right.

23 MS. TULL: Because the rule will be out.
24 Okay.

25 CHAIRMAN MALMUD: All right, Dr. Nag's

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1 request is for a full committee meeting. Is there a
2 second to the motion for a full committee meeting?
3 This will be teleconference. It's seconded. All in
4 favor? Any opposed? The motion carries. Thank you,
5 Dr. Nag. Thank you, Dr. Zelac, for the recommendation
6 and --

7 MS. TULL: I will e-mail everyone for
8 potential dates.

9 CHAIRMAN MALMUD: Terrific now, we go back
10 -- well, first I want to welcome Dr. Suleiman who has
11 joined us. He had other business which was urgent
12 this morning, and we were told he'd be arriving a
13 little bit later. We're glad to see you.

14 DR. SULEIMAN: I'm glad to see you're glad
15 I'm here.

16 CHAIRMAN MALMUD: Now, Dr. Howe?

17 DR. HOWE: The subcommittee has presented
18 its draft of the proposed changes to the gamma knife.
19 It's important for the NRC staff to know what the
20 Committee wants to do with this. So if you could give
21 us an idea of whether you want to have us include this
22 in a User Need Memo or any other action.

23 CHAIRMAN MALMUD: What is the Committee's
24 pleasure regarding the document, the draft of the
25 gamma knife document? Dr. Thomadsen.

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1 DR. THOMADSEN: I think the intent of the
2 subcommittee was to address the concern of the staff
3 that we present to them suggestions for how to make
4 the rules generic enough to fit all of these types of
5 units. So I would assume that the -- since this
6 committee set up the subcommittee to do that, that the
7 intent of this committee is that the recommendations
8 be propagated into rule.

9 CHAIRMAN MALMUD: We'll take that as a
10 motion. Is there a second to the motion? There's a
11 second to the motion. Any further discussion? All in
12 favor of the motion? Any opposed? Any abstentions?
13 The motion carries unanimously.

14 Thank you, Dr. Howe, thank you Dr.
15 Thomadsen and the hour being 11:50 we should adjourn
16 for lunch unless there is not a motion to do so. We
17 are adjourned for lunch. We will regroup promptly, if
18 we may, at 12:45. Thank you all.

19 (Whereupon at 11:51 a.m. a luncheon recess
20 was taken.)

21 6. BYPRODUCT MATERIAL EVENTS SUBCOMMITTEE REPORT

22 MEMBER LIETO: Since we are loaded up
23 here, I guess we can get started. My name is Ralph
24 Lieto. I am Chair of the Medical Radioactive Material
25 Events Subcommittee. We provided data preliminarily

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1 at the October meeting, and this was our Subcommittee
2 report.

3 Subcommittee members are Debbie Gilley,
4 Drs. Nag, Suleiman, and Thomadsen, besides myself.
5 And everybody had a piece of this patch to put into
6 the Subcommittee report. So we will get to the
7 specifics.

8 The report is based on the nuclear
9 materials event database, or NMED, based on the
10 government fiscal year 2007, which is inclusive of
11 those dates. And these are the report dates of the
12 event. So an event could have occurred outside this
13 time frame, but it was reported within this time frame
14 for inclusion in the report.

15 We broke the report down into categories
16 of events. And I want to emphasize that these are not
17 just medical events, but they are also radioactive
18 material events. So there are events that involve
19 medical use that did not necessarily meet the
20 definition of a medical event.

21 We broke the categories into parts based
22 on Part 35, Part 300, 400, 600, and 1,000 medical
23 events and then a fifth category, which involved other
24 medical radioactive material events.

25 A couple of observations in using the NMED

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1 database, some suggestions for improvement. We
2 thought these could be implemented, facilitate, and
3 search capabilities, as well as being more certain of
4 capturing events. And that would be to do reports or
5 queries by specific licensee type as well as also
6 being able to use multiple key words. Right now you
7 can only use one key word when doing searches in NMED.

8 Another observation -- and it really, I
9 guess, may be a point -- is that one of the other
10 Committee members indicated that very often reports do
11 not specify root cause or possible cause of the event.

12 Now that is not the fault of the database
13 because this is just I guess a report gathering, if
14 you will, of the events. And it's only as good as the
15 information that gets put into it by the reporting
16 agency, either Agreement State or region.

17 Looking at the first category of 35.300
18 events, which are unsealed radiopharmaceuticals
19 requiring a Written Directive, there were seven
20 events. Six involved I-131. One involved Y-90. Five
21 of those I-131 events were sodium iodide in the
22 treatment of thyroid therapy.

23 The type of errors and the subsequent
24 actions reported by the licensee are indicated on this
25 slide for the Y-90 and I-131 BexxarTM, which have

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1 similar types of clinical treatment purposes and a
2 couple of the I-131s. And as you'll notice in this
3 slide and in the next slide for the I-131 therapies,
4 the type of error was failure to follow the Written
5 Directive.

6 The observations in review of the
7 radiopharmaceutical therapy medical events that the
8 I-131 medical events were extremely small based on
9 2006 data that was able to be obtained for this type
10 of therapy, which was approximately 18,000
11 radiopharmaceutical therapies administered and the 7
12 reported medical events. This came out to an
13 estimated error rate of .04 percent.

14 Human error continues to be the main
15 factor for these medical events. And in an attempt
16 for this Committee to try to trend data, we compared
17 the report, the number of events for fiscal year 2007
18 to 2006. You can see that it decreased a little bit,
19 but probably from a statistical standpoint, it is
20 quite insignificant.

21 Probably in the preamble to the Committee,
22 this Committee report, I should mention this was the
23 first time that we have actually had a formal
24 Subcommittee report on medical events and that one of
25 the things that we're trying to do is track trends so

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1 that as we do subsequent reports, we will continue to
2 track the number of events that are reported and
3 report back to the Committee for potential future
4 action.

5 The next category was 35.400, which is for
6 manual brachytherapy. There were seven events. Six
7 of these involved prostate implants, seed implants.
8 One was a unique low-dose rate therapy application
9 involving dual radionuclides, cesium-137 and
10 iridium-192, in a patient.

11 And the type of error reported for the
12 dual isotope study involved incorrect source strength
13 being entered into the treatment planning computer for
14 this low-dose rate therapy. For the others regarding
15 the prostate implant, they were Mick applicator
16 malfunctions and four cases of incorrect source
17 placement into the prostate based on the imaging with
18 ultrasound.

19 If we look at the type of errors for the
20 manual brachytherapy, we see that failure to identify
21 positioning with ultrasound occurred in three of the
22 events, prostate implants, and in the other was the
23 patient movement and failure to reposition based on
24 ultrasound imaging and then again the applicator
25 malfunctions and the incorrect source strength being

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1 input into the treatment planning computer for the
2 low-dose rate therapy.

3 The observations, the common issue with
4 prostate implants was improper identification of land
5 boundaries by ultrasound, the observation being that,
6 even though it's beyond the scope of the NRC, the need
7 to assure adequate training and that imaging protocols
8 have been established in the use of the ultrasound
9 before the procedure.

10 Both Mick applicator errors were user
11 failure errors, not the failure of the applicator
12 itself. So, again, it gets to better user training
13 and practice with the Mick applicator being recognized
14 and that potentially if there are problems with
15 jamming applicators, it might be beneficial to have a
16 backup applicator as a standard of these types of
17 procedures being done.

18 The other observation, which relates to
19 the source strength issue, was that orders both by the
20 licensee and the manufacturer for radionuclide
21 implants, specifically the seed implants, need to
22 document both the Air Kerma Strength as well as any
23 other desired unit, whether it be apparent activity or
24 milligram radium equivalent. But it's the licensee
25 responsibility for verifying that the proper unit is

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1 input into the computer entry. The recommendation
2 here is that scientific societies consistently
3 recommend that the standard of use of Air Kerma
4 Strength be used and the need to reinforce this with
5 manufacturers and users.

6 And there is in process right now a draft
7 I believe it is Information Notice from the NRC that
8 will address this specific point. So action is in
9 progress.

10 These are a relatively small number of
11 medical events, again in almost all cases caused by
12 human error and demonstrating the need for adequate
13 training in these types of therapies.

14 As I go along, if any of the Subcommittee
15 members have anything to add on these points, just
16 feel free to chime in.

17 The next category is category 35.600,
18 which involved remote afterloaders in teletherapy.
19 This was a breakdown for fiscal year 2007 versus 2006.

20 There was only an increase of three medical events
21 for all these uses.

22 Regarding all HDR, there was an increase
23 by two, the medical events. The breakdown for the HDR
24 because in the past, it had been broken down into
25 MammoSite® uses versus other HDR medical events, the

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1 Subcommittee further broke this down also into the use
2 for vaginal cylinders, which had -- this was not
3 reported in the previous medical event I guess I
4 should say summary that we did in the fall for 2006
5 events, but the Subcommittee felt that this was
6 important to specify as a separate item because
7 vaginal cylinder implants are usually considered the
8 simplest, most standard type of HDR application for
9 these types of devices.

10 And when you look at the numbers of HDR
11 events, we have on their five or possibly seven.
12 Because of the way the report was written, we couldn't
13 determine for sure, although the way the summary was
14 specified, it seemed to imply that in two cases that
15 involved vaginal cylinder applications, that it's
16 anywhere from a third to almost half of the medical
17 events involving HDR applications.

18 There was one event involving LDR remote
19 afterloader and two with **GammaKnife?MammoSite™** and
20 none with other teletherapy devices.

21 MEMBER NAG: You asked me to comment.
22 Maybe I can comment here. The vaginal cylinder is
23 simple. And what that means is not that you make more
24 mistakes on the simpler ones.

25 What I think it means is that people who

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1 do HDR very infrequently only do vag cylinders. They
2 don't go into the more complex one because it requires
3 sedation or operating room and so forth.

4 So usually those who don't do too many
5 HDRs only do vag cylinder. And that is why you are
6 seeing a higher proportion of mistakes in the vag
7 cylinder because it's done by people who are doing
8 very few of them; whereas, those who do the other kind
9 of implant have more practice in HDR brachytherapy.

10 MEMBER LIETO: Thank you.

11 In looking at the HDR events, this
12 Subcommittee broke it down based on the two vendor
13 devices that are used. For Nucletron, there were
14 eight events. And the various errors that resulted in
15 the medical event are indicated as well as whether the
16 application was for vaginal cylinders or for
17 MammoSite™.

18 The other vendor is Varian. There were
19 six events, again with a breakdown based on whether it
20 was vaginal cylinder or HDR. And if it's not
21 indicated, it meant that it was neither of those
22 applications that resulted in the error.

23 Looking at the vaginal cylinder breakdown,
24 you can see that the causes were wrong, step size
25 wrong, isodose being selected, wrong catheter length

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1 being entered in the treatment planning, fluid in the
2 source track, improper default length used.

3 So, again, the emphasis that the
4 Subcommittee wanted to indicate is that, even what is
5 considered the most simplest treatment in the use of
6 HDRs does result in a fair number of medical events
7 overall in the use of HDR.

8 MEMBER VETTER: Could I ask a question?

9 MEMBER LIETO: Sure.

10 MEMBER VETTER: These data came from NMED.

11 MEMBER LIETO: Right.

12 MEMBER VETTER: Does anyone on the
13 Committee have any idea how many events may have
14 occurred that didn't qualify as a medical event; in
15 other words, smaller errors that would have been
16 addressed by quality control within radiation oncology
17 but that --

18 MEMBER LIETO: That didn't result in a
19 medical event?

20 MEMBER VETTER: To further suggest that
21 maybe additional education or something is required.

22 MEMBER WELSH: Well, isn't that what is
23 meant by the abnormal occurrences on the last slide?

24 MEMBER VETTER: No.

25 MEMBER WELSH: Separate?

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1 MEMBER VETTER: No. So the answer is no,
2 I guess?

3 MEMBER LIETO: The answer is no the best I
4 can tell. Debbie?

5 MEMBER GILLEY: However, they're supposed
6 to document with recordable events different than
7 medical events, but there's not a registry of
8 recordable events out there. But as part of the
9 quality management program, they're supposed -- isn't
10 that correct, Donna-Beth?

11 DR. HOWE: For the NRC, we no longer have
12 recordable events. We just have reportable events.
13 And we did away with the name "quality management
14 program." And so it doesn't have quite the
15 requirements it had before.

16 MEMBER GILLEY: So there are not
17 recordable events at all for things that didn't --

18 DR. HOWE: Not in NMED.

19 MEMBER GILLEY: Not in NRC regulations.

20 MEMBER VETTER: Correct. Yes. I think
21 the only way you would get this would be directly from
22 the radiation oncology community. And I guess the
23 only way would be if they were actually reporting this
24 at meetings. So the answer probably is no.

25 MEMBER NAG: Yes. They won't be because

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1 if there are minor errors, less than 20 percent,
2 previously, as we said, 10 percent was a reportable
3 event, and that information would have been filed.
4 But now it won't.

5 MEMBER VETTER: Correct.

6 MEMBER NAG: But usually if there is going
7 to be a problem with selecting the wrong length or
8 selecting wrong spacing, you are going to be having
9 errors that are going to be much smaller than 20
10 percent.

11 And if it is an error, 25 percent or
12 something like that, that was within the range of what
13 is clinically acceptable.

14 MEMBER SCHWARZ: I have a question.

15 CHAIRMAN MALMUD: Yes?

16 MEMBER SCHWARZ: I'm curious about total
17 numbers of these procedures. I mean this as compared
18 to radiopharmaceutical misadministration kinds of
19 information. I mean, it is always a curious question
20 because these numbers are very small.

21 MEMBER LIETO: Yes.

22 MEMBER SCHWARZ: And if we had an idea of
23 a denominator, it would be helpful.

24 MEMBER LIETO: I appreciate that preamble
25 because it is going to get to my next slide.

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1 MEMBER THOMADSEN: Donna-Beth has --

2 CHAIRMAN MALMUD: Donna-Beth?

3 DR. HOWE: I just want to make an
4 additional comment. And that is that if there is
5 something that is considered a device failure, then
6 those are reported under 30.50 or part 21. And Ralph
7 I believe discussed those in the October meeting.

8 So those are things that didn't involve
9 patients but may have been picked up during the
10 quality control type of procedures. So we do have
11 some additional information, but it's not on --

12 CHAIRMAN MALMUD: Thank you.

13 MEMBER LIETO: Regarding the gammonite,
14 there were two events. One was wrong isodose being
15 selected into the treatment plan, and another was the
16 images were reversed and the wrong side of the patient
17 was treated.

18 The overall for 35.600 events, three types
19 of errors stood out specifically for the HDR, which is
20 a predominant type of medical event that occurred, was
21 wrong length being entered in, either for catheters or
22 starting points, wrong plan being entered, wrong dose
23 being entered. So it was in that treatment planning
24 phase for the events.

25 Vaginal cylinder, surprisingly, dominated

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1 the number of events considering they're considered to
2 be the more simpler type of events. To get to Dr.
3 Schwarz's comment about do we have any statistics,
4 based on 2006 data, it's estimated that 32,000
5 patients were treated with 35.600 applications.

6 With an average of 5 fractions per course
7 of treatment, this results in about 160,000 treatment
8 fractions. And with 17 failures of that over those
9 number of opportunities, it comes out to an error rate
10 of about .01 percent, which is, shall I say, in the
11 same order of magnitude as what we reported for the
12 iodine-131 therapies.

13 So applying some statistics that I believe
14 Dr. Thomadsen is going to be addressing in his
15 presentation a little bit later, the field is
16 operating at what is called a 5.2 sigma operational
17 level, which is considered very good. And I guess six
18 sigma, which is an area where nobody in medicine
19 operates at, would indicate that this would be a level
20 of about three failures.

21 MEMBER NAG: Can someone tell me what
22 sigma means? I'm sorry to be so naive.

23 CHAIRMAN MALMUD: Standard deviations of a
24 mean. So within 2 sigma would be 95 percent on both
25 sides of the curve.

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1 MEMBER VETTER: So six sigma would be way
2 out.

3 MEMBER THOMADSEN: You may have heard in
4 industry, they deal with six sigma as trying to
5 improve the quality. That's the goal as to get out
6 that. Nobody makes it. Well, the airlines.

7 CHAIRMAN MALMUD: Well, the airlines do.

8 MEMBER THOMADSEN: Airlines.

9 CHAIRMAN MALMUD: Because if the airlines
10 have a .01 percent accident rate, a 1 in 10,000
11 flights would be gone.

12 Was your question answered?

13 MEMBER NAG: Yes, but one additional
14 comment. I think we have to also mention that in the
15 airline, if you have a failure, it almost always means
16 death; whereas, here, yes, you are having an abnormal
17 occurrence or a medical event.

18 What percentage of that is dangerous? You
19 know, we have to take that flight into account or,
20 when possible, leading to death? You know, of these,
21 we have how many, you know, whatever number? Of that,
22 how much is it really concerning?

23 CHAIRMAN MALMUD: You're correct. And of
24 these, it may very well be that none results in death.
25 And it's possible that none results in a significant

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1 medical complication.

2 However, because the outcomes are
3 time-related, it is difficult to say with certainty
4 what the morbidity and mortality are. And, therefore,
5 we are constantly working at improvement, as we all do
6 every day, as you do in your practice and I do in
7 mine.

8 So we aim for perfection. And we are
9 human, and we don't achieve it. But we still aim for
10 it.

11 MEMBER SCHWARZ: And I had asked Ralph on
12 the side here just where the numbers for the total
13 population came from. And he said that they had come
14 from Medicare.

15 MEMBER LIETO: I believe there is -- or is
16 it reporting?

17 MEMBER THOMADSEN: Most of it actually
18 comes from a company called BMI, who does surveys of
19 facilities. This data was from a survey. We sent out
20 surveys to 7,000 institutions, clinics, which actually
21 replied, which is an incredibly good number. So we
22 have pretty good data now on the number of patients.

23 MEMBER LIETO: And probably we also should
24 point out the denominator for the fraction of this is
25 2006, although the fiscal year numbers and the

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1 numerator for 2007, the presumption is that the
2 denominator is going to change that dramatically from
3 2006 to 2007.

4 But, even if it did increase, that just
5 would reflect that the fraction would be slightly
6 smaller.

7 MEMBER THOMADSEN: And, actually, much of
8 the data, the 17 failures, were in 2006.

9 MEMBER LIETO: Good point. Any more
10 questions on --

11 CHAIRMAN MALMUD: Any questions for Mr.
12 Lieto?

13 (No response.)

14 MEMBER LIETO: I'll go on to the last
15 category of events, which were the 35.1000 events and
16 other radioactive material events. In the part 35
17 other events, these would be medical events that
18 involved patients that are being treated with
19 applications that are listed under 35.1000, which is
20 principally the microspheres and reports, fetal/embryo
21 dose from patients who received radiopharmaceuticals
22 while being pregnant,

23 The fetal embryo dose is not under the
24 definition of a medical event. And that's why it's
25 under this other category. And then also included was

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1 other reportable medical events into the NMED that
2 involved the medical use of radionuclides. There were
3 15 of these events.

4 And I think that needs to be corrected on
5 your slide. I think I had the wrong number there on
6 your slides. That should be 15. In that 15 events, 6
7 of these were loss sources. Three were leaking
8 sources. Three events involved contaminated licensee
9 packaging and then three, which I put into this
10 miscellaneous category because they were kind of
11 unique and didn't fall into anything or the other.

12 The 1,000 uses were all microsphere
13 events. Eight of the events related to problems with
14 the equipment used and administration, and two of the
15 events involved miscalculation of the absorbed doses
16 or dosages that were administered.

17 The other 35 events were the 2 pregnant
18 patients that were administered I-131 therapies. In
19 the one event, the patient was 13 to 15 weeks pregnant
20 and was administered 15 millicuries of sodium iodine.

21 In the other, the patient was 4 to 5 weeks pregnant
22 and was administered 125 millicuries. And the people
23 dose estimates are as indicated in the NMED reports
24 that are specified there.

25 In terms of other material events, there

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1 were the six events involving lost sources. Four of
2 these events involved prostate seed implants that were
3 lost. One case was a breast tumor localization. The
4 other three were after prostate implants.

5 Another was sources of unknown origin were
6 found in a locked hospital X-ray room cabinet in a
7 hospital that was not licensed for radioactive
8 materials. And the other event was a cesium-137
9 low-dose brachytherapy source that was lost after
10 being removed from the patient but subsequently found
11 in the hospital laundry.

12 The leaking sources, there were three
13 events. There were two events that came from the same
14 licensee. They were somewhat apart by a significant
15 amount of time, involved I-125 brachytherapy seed
16 containers that were wiped and found to be
17 contaminated above removal contamination limits.

18 The therapies were subsequently postponed
19 and the sources returned to the manufacturer. In one
20 of the reports that did indicate a follow-up from the
21 vendor, that indicated that there was a faulty weld
22 found on one of the seeds.

23 In another event, the seeds, which is not
24 I think a common practice, were leak tested before
25 implant. And removal contamination was found four

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1 times that allowed for for removal contamination from
2 a sealed source.

3 The other event involved contaminated
4 packaging. I would kind of lump this as one event,
5 even though there were three incidents from the same
6 licensee, shipments from a centralized pharmacy having
7 surface contamination on the package being received
8 above reportable limits. No cause was specified in
9 these events.

10 And then the other miscellaneous, one was
11 a teletherapy malfunction. And this was I think one
12 of the events that Dr. Howe was referring to where the
13 source stuck in the open position failed to retract.

14 Staff responded promptly based on training
15 for emergency intervention, returned the source into a
16 shielded event. And, as a result, the patient
17 unexpected dose did not exceed 20 percent. But this
18 would be reported not as a medical event but as an
19 event under 35.50.

20 And then another on a sort of I'll say
21 unique event involved a number of individuals who were
22 given diagnostic agents involving chlorine-18 and
23 technetium-99m for purposes of training employees and
24 evaluating new imaging equipment. They exceeded the
25 dose levels allowed for members of the general public.

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1 And, as a result, this was reported by the Agreement
2 State.

3 In summary here, listening the materials
4 events, comparing fiscal year 2006 versus 2007, we see
5 a significant increase in the number of events being
6 reported for the Y-90 under 35.1000, an increase on
7 the embryo fetus dose. I guess you could say it
8 doubled, even though it only increased from one to
9 two.

10 The loss sources and leaking sources were
11 fairly constant or decreased. And, as I mentioned, we
12 lumped in the miscellaneous events of the contaminated
13 package as a single event. So when you look at these
14 miscellany events, they either decreased or were
15 fairly constant.

16 Overall there were 19 events in fiscal
17 year 2006 versus 25 for fiscal year 2007. Now, we
18 wanted to try to trend this also to look at medical
19 events over the last four years because in the NMED
20 report, fourth quarterly report, there are statistics
21 that indicate the number of events over a 16-quarter
22 period.

23 When we looked at these, just summed these
24 up into annual totals, as you can see, the medical
25 events seem to be fairly constant over the four-year

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1 period. What we are maybe looking at is just the
2 natural variance in an uncommon event that occurs over
3 that time period.

4 The other thing we wanted to compare it to
5 was also the medical abnormal occurrences that are
6 reported. Now, an abnormal occurrence, which is going
7 to be discussed a little bit later by Angela, are the
8 most significant events, medical events, that occur.
9 They have to be above a much higher threshold than
10 required for medical events. And these events are
11 reported to Congress on an annual basis. So these are
12 sort of the most significant of the medical events.

13 Now, one of the things that I would like
14 to indicate is that in the abnormal occurrences, this
15 would include like not only the significant medical
16 events but also the embryo fetus dose events. The
17 medical events that are reported in the NMED report do
18 not include in them events that involve the embryo
19 fetus doses because they are not "considered medical
20 events." So just kind of be aware of the differences
21 in some of the numbers that go into that.

22 The abnormal occurrences might indicate
23 that there is an increasing trend, but, again, this
24 might just be a variation in a very small number of
25 events that we're seeing over this time period.

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1 Probably the final point that I wanted to
2 make is that in terms of the medical events, it's not
3 necessary that one medical event involves one patient.

4 So a single medical event could actually involve a
5 single report of a number of patients. And I know
6 that is the case in some instances regarding the
7 brachytherapy seed medical events that have been
8 reported in the past.

9 And I think that is the last slide. So
10 the Subcommittee and I would be glad to entertain any
11 questions.

12 CHAIRMAN MALMUD: Thank you, Mr. Lieto.

13 Are there any questions for Mr. Lieto or
14 comments from other members of the Subcommittee?

15 MEMBER SULEIMAN: I have a question,
16 clarification.

17 CHAIRMAN MALMUD: Excuse me.

18 MEMBER SULEIMAN: I don't know why I
19 didn't ask it earlier, but the misuse of the
20 radiopharmaceuticals for training purposes, who cares
21 what the threshold is? That's just improper. There
22 are regs that that is a violation of.

23 Donna-Beth? In other words, what if the
24 doses were below 100 millirem? Who cares? What was
25 done was inappropriate. It was unethical. I thought

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1 state --

2 MEMBER GILLEY: As part of the radiation
3 protection program, they are required to keep doses as
4 reasonable as possible. We would take action. So I
5 don't know what this particular state did, but it
6 would be a failure to --

7 CHAIRMAN MALMUD: Donna-Beth?

8 MEMBER SULEIMAN: The trigger shouldn't be
9 what they find. The sheer fact that they did that was
10 incorrect.

11 CHAIRMAN MALMUD: Donna-Beth?

12 DR. HOWE: Generally we find out about
13 these events because of allegations. And then we look
14 at violations and we find it's not a medical event.
15 And then we find out that we find some other violation
16 that we can tag it to. And then we generally find out
17 that it's willful.

18 So there is not, per se, a reporting
19 requirement for this. We generally find it out after
20 the fact through allegations. We do have a public --

21 MEMBER SULEIMAN: Would these really
22 qualify as medical events or --

23 DR. HOWE: No.

24 MEMBER SULEIMAN: No.

25 DR. HOWE: No. And they're not reportable

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1 as medical events. And that's one reason we find out
2 about them primarily through allegations.

3 MR. LEWIS: Just to be clear, if it had
4 been below the public dose limit. But these were
5 above it and would be reportable under part 20.

6 MEMBER GILLEY: These were diagnostic.
7 These were diagnostic bases.

8 MR. LEWIS: Diagnostic.

9 MEMBER GILLEY: They don't qualify.

10 MR. LEWIS: They were over 100 millirem?

11 MEMBER GILLEY: None of them were.

12 DR. HOWE: It's not the public dose limit
13 because the public dose limit is the licensee is not
14 supposed to have its problem so that it gives the
15 member of the public an access. These are deliberate
16 acts.

17 MEMBER SULEIMAN: Nonmedical use.

18 DR. HOWE: Nonmedical use.

19 MEMBER GILLEY: Or not the public.
20 They're occupational workers. The standard is
21 different.

22 DR. HOWE: But they're not permitted these
23 doses under the normal occupational levels either. So
24 we don't have a specific regulation that says, "You
25 will not irradiate people." But we do get it through

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1 violations and allegations.

2 CHAIRMAN MALMUD: Dr. Eggli?

3 MEMBER EGGLI: Actually, though, I think
4 there is a specific regulation that says a dose
5 administered has to be for medical use. So I don't
6 remember exactly where it is, but I think it is out
7 there that any radiopharmaceutical administered has to
8 be for medical use.

9 CHAIRMAN MALMUD: It is. Mr. Eggli?

10 MEMBER GILLEY: It has to be all the data
11 if there were a clinical procedure with a clinical
12 procedures manual or it has to be a written order from
13 an authorized user. Those are the two mechanisms.
14 You either use a clinical procedures manual or you can
15 use a --

16 CHAIRMAN MALMUD: I suspect that in our
17 state, it is a violation of the Pharmacy Act because a
18 radiopharmaceutical as a pharmaceutical requires a
19 prescription. And these individuals would have been
20 administered pharmaceuticals without permission,
21 without prescriptions.

22 MEMBER EGGLI: And I think in some of the
23 cases where you are looking at -- this is Eggli --
24 administrations for testing equipment, that first in
25 most dose ranges, a written directive wouldn't be

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1 required, but in clinics where there is a practice to
2 do a written directive, the written directive probably
3 would have been written.

4 I think that there are a lot of practices
5 out there who, in fact, don't understand that you
6 can't administer radioactive materials just to test
7 new equipment. You can sort of give away tests to
8 people who have medical indication when you are
9 testing new equipment, but you can't recruit folks,
10 normal volunteers, without a research protocol.

11 And in most states, although it's not an
12 NRC regulation, the same is true for CT or any form of
13 ionizing radiation, that normal volunteers cannot be
14 studied. But, yet, I think most end users are
15 probably unaware of that.

16 CHAIRMAN MALMUD: Any other questions or
17 comments? Yes, Mr. Lieto?

18 MEMBER LIETO: I just want to again thank
19 my Subcommittee members for their support and aid.

20 CHAIRMAN MALMUD: Can you name them for
21 us, please?

22 MEMBER LIETO: Yes, Debbie Gilley, Dr.
23 Thomadsen, Dr. Suleiman, and Dr. Nag.

24 CHAIRMAN MALMUD: Thank you. That's for
25 the record. Thank you.

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1 And if that completes your report?

2 MEMBER LIETO: Yes. We have no
3 recommendations for Committee action.

4 CHAIRMAN MALMUD: Thank you very much.

5 We will now move on to the next item on
6 the agenda, which is "Causes of Medical Events." Dr.
7 Thomadsen?

8 MEMBER THOMADSEN: You could just pass
9 that along.

10 CHAIRMAN MALMUD: We are going to have a
11 handout?

12 MEMBER THOMADSEN: Thank you.

13 7. CAUSES OF MEDICAL EVENTS

14 MEMBER THOMADSEN: One of the goals of my
15 presentation is to discuss root causes of errors. And
16 so we should start by looking at what is a root cause.
17 To that, we should look at two divisions of failures
18 that happen.

19 There are failures that are results of
20 active errors; that is, something that somebody does.

21 Somebody commits an act. And because of that,
22 something bad happens. Then there are latent errors,
23 which are the organizational or environmental
24 conditions that lead an individual to fail.

25 Latent errors have certain

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1 characteristics. Active errors usually only affect
2 the particular patient -- while that is what people
3 say -- while latent errors can affect all the
4 patients.

5 This isn't really true. An active error,
6 such as an incorrect calibration from a machine, could
7 affect a large number of patients while a latent error
8 might only lead to an event that injures one or maybe
9 never anybody.

10 Most often, though, it is true that active
11 errors are a one-time, one-patient thing and latent
12 errors are systemic errors, which form traps that
13 people fall into. And that leads people to make an
14 active error. Latent errors often are things like
15 lack of staffing or the policies or training
16 practices.

17 Usually you would like to do a root cause
18 analysis of events and find latent errors because that
19 way you could fix the system. They are often very
20 hard to find.

21 Also you often find that latent errors are
22 things that are very hard to change. They are built
23 into the organizational structure as a large
24 hierarchy. And that is not likely to change or their
25 attitudes in the administration, which are not going

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1 to change.

2 But you would like to find latent errors
3 if you can because that way you might be able to
4 change something that might lead to a lot of different
5 errors. And fixing the latent errors, however, is not
6 necessary to fix the problem. And we'll get to that
7 in just a little bit.

8 If we're doing an event analysis, very
9 often we'll start with a process tree or a process map
10 that helps understand the process. And then we do an
11 FMEA that is a failure modern event analysis. But
12 when we're setting up our process, we understand what
13 could happen and try to prevent that.

14 And, just like we have the process tree
15 when we're setting up a process in the first place,
16 although most people don't go through that, after
17 there is an event, we do an event analysis diagram
18 just to help us understand the event. That is all it
19 is for.

20 The diagram is often built by a team,
21 which can take a long time with a lot of arguing, and
22 people disagree or sometimes it is done by an
23 individual, which leads to the problem that the
24 individual may not understand parts of the event or
25 misinterprets something.

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1 As I say, the main tool in the root cause
2 analysis is a root cause analysis tree, an RCA tree,
3 or diagram, which starts at the top with the event at
4 the top of the box. And then you ask, what actions
5 immediately preceded the event? What caused it right
6 at that moment? And these actions are boxes just
7 below the event, usually going by a fault tree.

8 So here is an example of a fault tree
9 where somebody fell down the stairs. And cause, the
10 immediate cause, was that person was carrying laundry
11 and couldn't see that there was a cat sitting on top
12 of the stairs. And so you have two immediate causes.

13 If you took away either of those causes,
14 you would not have had the event, which is why they go
15 into an entry. Both causes had to be there
16 simultaneously or the event wouldn't have happened.
17 If you took away one of them, you interrupt the
18 propagation of the error, which either one of those
19 could be.

20 Immediate causes are called the proximal
21 causes. For each proximal cause, you go around. And
22 you ask, well, what caused that? And you keep asking,
23 "What caused that?" as you build the tree. And you
24 keep going down until you get to the last action over
25 which you had control.

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1 The causes for that last action, being out
2 of your control, are of no interest to you. So you
3 define that as your universe. You stop asking the
4 questions after you get to the point where you no
5 longer have control.

6 For an example, to try and define where
7 the edge of the universe is, if the power utility has
8 an outage and in the hospital, the surgeon in the dark
9 cut off the patient's head, you don't care why the
10 power utility lost power. You couldn't affect that if
11 you wanted to. So you stop asking at that point.
12 That is outside of your universe.

13 You do care what actions take place in the
14 hospital that led to the surgeon cutting off the
15 patient's head. That is within your range of control.

16 So your universe is drawn where you can have control
17 over things and you can't.

18 Progenitor causes are those things at the
19 beginning of each of those paths, the first thing
20 inside of your universe that led to the pathway that
21 eventually caused the event. The progenitor cause may
22 be a root cause or it may just be a condition.

23 An example of a condition would be the
24 primary nurse who was supposed to be taking care of
25 something was home sick. There isn't anything you

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1 could or would do about that. That's not a cause per
2 se. It is a cause, but it is not a cause that you are
3 interested in. So it is not a root cause or in our
4 simple example, the cat sitting on the top of the
5 stairs was just a condition.

6 And it's not something that you
7 necessarily will do something about. I suppose if you
8 change your cat, then the cat wouldn't have been
9 there.

10 In the diagrams, often progenitor causes
11 are shown as ovals.

12 We want to find root causes, but the whole
13 concept of root causes is not clear. It sounds
14 wonderful, and it sounds like something you would want
15 to do.

16 What we're looking for with root causes
17 probably are those things that you can change that
18 would prevent events of a similar nature. You would
19 like them to be latent errors; that is, situations in
20 the organization that facilitate failure initiation
21 and propagation. You often find active errors; that
22 is, something somebody did.

23 The very fact that most of the time we've
24 got these and gates implies that there is no root
25 cause. There is no one thing that caused anything.

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1 You had to have a set of conditions.

2 The environment is often a contributing
3 factor. And that enters the tree from the side,
4 through a diamond, just sort of like a transistor.
5 Here we have a cat sitting at the top of the stairs.
6 There is an environmental condition that the light was
7 low. And so somebody tripped over the cat. That is
8 not so much seen as a cause as a condition. But we
9 will see that those types of conditions need to be
10 fixed right away.

11 What do you do? Sometimes a progenitor
12 cause is a truly latent cause but may be too hard to
13 fix. But one shouldn't worry about that because to
14 prevent the events, all you need to do is set up
15 something that will interrupt the propagation of a
16 failure. You don't have to cure all the problems.
17 All you have to do is set up systems that will
18 interrupt the flow.

19 This is a rather famous illustration from
20 James Reason's book *Human Error* that is shown in
21 almost all talks on error propagation, showing that
22 you've got all sorts of levels of defense in any
23 system that you have, any organization, where you try
24 to prevent things from happening. But almost all
25 defenses have holes in them. And if all the holes

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1 happen to line up, then you can have the event
2 propagate right through it.

3 Of course, what you need, you need to have
4 the event be initiated at the beginning, and you have
5 to have these holes all line up. So it's a complex
6 situation that very rarely happens, but it does
7 happen. And this is what you try to prevent.

8 You can prevent the error by looking at
9 the beginning or by just changing any of those
10 defenses so you no longer have the holes line up.

11 This except it's gone off the bottom is an
12 example of a root cause analysis tree just showing
13 they do get somewhat complex. You see it starts at
14 the top.

15 We are joined by an and gate. Almost
16 every root cause analysis I've ever seen has an and
17 gate right under the event. Humans are one deductive
18 and can handle something that goes wrong.

19 The problem is when something goes wrong
20 and something else goes wrong. When we have got two
21 things happening at once, then it is a problem. And
22 that's when events actually happen.

23 And you can see that each event on the
24 left side as you go down has an and gate right after
25 it because, once again, each of those steps probably

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1 by themselves could be handled quite well by anybody.

2 But when you put them together with other things,
3 people have problems.

4 The difference you can almost see, you
5 can't see in your slides, in your book but on the
6 screen, you can maybe make out. But at the bottom,
7 some of those ovals because the progenitor events are
8 a darker yellow and some are a lighter yellow. The
9 light yellows are those that are just conditions, and
10 the darker yellow are actually progenitor causes that
11 you could do something about, that you might be able
12 to fix.

13 The small text -- I'm not expecting you to
14 read any of these. And, particularly on the handout,
15 you can't read anything. But the small black text off
16 to the side of some of the boxes is looking at what
17 the classification of those boxes would be, those
18 failures in the boxes, if you were looking at them
19 with certain taxonomies, which are useful for trying
20 to classify types of errors.

21 This is just another one. It's easier to
22 see in your book than on the screen, where the color
23 black gets blended in with the dark blue. But those
24 arrows are pointing to where a cause actually feeds
25 into two sides of a tree.

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1 And usually when we're looking at these
2 trees, if you've got an and gate, that actually means
3 you had different levels of defense where you had the
4 failure. And, in general, you probably would be
5 fairly good.

6 Here when you've got a cause that feeds
7 into two sides of the tree, that means that you
8 actually are doubling the likelihood that something
9 would go wrong. And that's a real hazard when you
10 analyze these things.

11 If we look at what to do, all failures
12 actually are system errors because the system didn't
13 prevent the propagation of the error. So, even if the
14 causes are active errors where somebody did something,
15 the system should be set up to be robust against that
16 and interrupt the propagation of the error.

17 All failures are human errors because
18 somebody did something wrong. And all the latent
19 errors are human errors because somebody made a bad
20 decision somewhere.

21 If you had, as I talked about earlier, a
22 machine calibration where you injured a lot of
23 patients, that was a systemic error. But it was an
24 individual who did it. So it is an active error also.

25 So even the definitions of latent errors,

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1 active errors, system errors, and sporadic errors are
2 very interrelated. It depends how you're looking at
3 them as to what the definitions actually mean.

4 Latent errors, as I have mentioned several
5 times, are usually very hard to fix. They are often,
6 as I say, like trying to make somebody change their
7 religion. They are built into the operations of your
8 organization.

9 The prevention of similar events can be
10 done by either eliminating the progenitor causes or by
11 interrupting the propagation. Often the interruption
12 is much easier to do.

13 If you look at this, are root causes
14 always latent errors? No, they are not. Are root
15 causes always progenitor causes? Actually, no. No,
16 they aren't. Are progenitor causes root causes?
17 Absolutely not.

18 For an event where a dosimetrist entered
19 the wrong dose, the root cause is not that the
20 dosimetrist entered the wrong dose. That's just part
21 of the event. And if we look at NMED and try to call
22 out from NMED what is the root cause, unfortunately,
23 you often see this type of inscription. The cause of
24 the event is the dosimetrist entered the wrong dose.

25 The root cause, if there is any such

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1 thing, is why the dosimetrist entered the wrong dose
2 and why such an entry propagated to the patient.
3 Those are the questions. And the root cause is
4 somewhere underneath there.

5 Patient intervention is never a root
6 cause. If we see that in an event, that is not
7 considered a real event because there was patient
8 intervention. That is not a viable explanation
9 because why. Why does the system allow something, an
10 untrained patient, and do that will propagate into an
11 error? Why don't you have something set up to
12 prevent?

13 A common example if you look into the
14 bronchial treatments, it will be that the event is
15 that are reported often is the patient has pulled out
16 the catheter. Why is the catheter not sutured in
17 place? Why is it not taped better? Why don't you
18 watch the patient better?

19 NMED reports almost never give enough
20 information to actually determine the causes, almost
21 never give an indication of whether the corrective
22 action is likely to work, which is a whole other
23 discussion. They do give the model number and
24 strength of the sort, which is usually pretty
25 irrelevant to the discussion at hand.

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1 If we look at error-preventing techniques,
2 this is information from the Institute for Safe
3 Medical Practices. There are different levels of how
4 effective a remedial action could be. The most
5 effective are the forcing functions up at the upper
6 left; that is, interlocked barriers, computers with
7 feedback, followed by automation and computerization,
8 bar codes, monitoring. Protocols are a big cut down
9 on there. Check sheets and alarms, they're good.
10 They aren't anywhere near like forcing functions.
11 Redundant checks come at the next level. Rules and
12 policies are pretty near the bottom. And at the
13 bottom is education. Particularly of interest, we
14 will see in reports of events, remedial action is to
15 train individuals.

16 The last thing, before I go to the next
17 slide, environments always should be corrected. I
18 think the next slide, policies that don't or things
19 that don't work. Policies usually are not an
20 effective way to correct things. They're the most
21 common thing you see. Particularly at my hospital, if
22 there is a problem, the first thing they have to do is
23 write a new policy.

24 Retraining. This is the education that we
25 were just talking about. If there was initial

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1 training, if people were trained, retraining them
2 never does anything. They know what they are to do.
3 They know what they are to do.

4 There was an editorial in the newspaper
5 back when there were civilians who were shot in Iraq.

6 The military's response was to retrain people. And
7 the editorial was it isn't that these people didn't
8 know better. It's that they didn't do that and
9 likewise in our events. The problem is people didn't.

10 It isn't that they didn't know. All of these people
11 knew. They just didn't do what they were supposed to
12 do.

13 Supervision. Adding supervision to the
14 job doesn't work. Expecting physicians to do more
15 than check the client, despite the fact that they are
16 the authorized users, they really don't know very much
17 about what is going on. And any type of remedial
18 action placing burdens on them is not effective.

19 Having people pay more attention, that's
20 the least effective of these things. That does not
21 work. Interestingly, the survey a few years ago
22 amongst physicians as to what is the most effective
23 way to prevent errors, 48 percent of the physicians,
24 48 percent of the different options they were given,
25 said physicians have to pay more attention. I don't

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1 know if they are assuming they aren't paying attention
2 now.

3 That is the end of the talk for now.
4 Another talk for the future -- actually, I see from
5 the billing that I got on the table that Ashley went
6 over this morning we are to talk about what things
7 should be in the NMED database. And, actually, I was
8 given a half-hour. That would be about another
9 half-hour talk to look at what would be useful as far
10 as classifications.

11 I think questions? Subir?

12 MEMBER NAG: You think that would work?

13 MEMBER THOMADSEN: Yes.

14 MEMBER NAG: How about saying, what do you
15 think are things that will work that way? And then
16 I'll go to the next comment. Do you have anything?

17 MEMBER THOMADSEN: Yes. The things that
18 would work are essentially we have lost data. That
19 was on the previous slide the priority error
20 prevention technique, the institute of safe medical
21 practice. Forcing functions, setting up systems that
22 somebody just can do something wrong. If you have it
23 interlocked, if you have a barrier that they can't get
24 through, they aren't going to make those mistakes.

25 There's a big jump when you get to bar

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1 codes because there has been a whole slew of medical
2 events, medication events with systems that use bar
3 codes because what nurses have done -- and you have to
4 build a forcing function into the bar codes to make
5 them safe -- is when they have the doors open, they
6 pull out extra medications that they think they are
7 going to need during the day so they don't have to go
8 back and do all the bar coding.

9 So forcing functions are the most
10 effective. That is what works the best.

11 MEMBER NAG: The other comment is from a
12 practical standpoint -- I know you give more of a
13 scientific slant. From a practical perspective, what
14 I have found looking at my own practice and others
15 around the country that I review, the one thing is
16 that those who were doing a lot of the same kind of
17 practice, I have found less errors or less abnormal
18 occurrence in those practices. So repetition
19 minimizes the error.

20 I don't know how to incorporate that in
21 there. But that from a practical standpoint is very,
22 very effective.

23 MEMBER THOMADSEN: Yes. On the paper that
24 is copied after the slides, when we looked at
25 brachytherapy events during the period, whatever the

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1 period was, one of the things we found, which was not
2 a surprise at all, is new procedures are dangerous.
3 That is when you have things going on with people who
4 aren't used to what they are doing.

5 We found that, interestingly, what would
6 make a new procedure was not only that it was new
7 somewhere. It could be somebody who has done this
8 many times at a different hospital, moves to another
9 hospital.

10 It was the first time at that hospital.
11 Actually, the first time isn't always the most
12 dangerous because everybody is watching like a hawk --
13 it is the second or third -- or it can be a hospital
14 that has done the procedure a lot and there is a new
15 physician coming to do it.

16 And the other thing the handout with the
17 Joint Commission points out is an incredibly dangerous
18 time when somebody is doing a procedure and passes the
19 patient off to somebody else, in which case that
20 patient is new to somebody who wasn't there for the
21 end of it.

22 Oh, yes, absolutely. The unfamiliarity is
23 terrible.

24 CHAIRMAN MALMUD: Thank you.

25 Dr. Vetter?

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1 MEMBER VETTER: I don't know if it's safe
2 to assume, but --

3 MEMBER THOMADSEN: It's probably never
4 save to assume.

5 MEMBER VETTER: Right, right. But many or
6 some of these medical events may have been reported as
7 sentinel events within the hospital, in which case the
8 Joint Commission requires that a root cause analysis
9 be done. I don't know if we can get plugged into that
10 or if we can get information from Joint Commission,
11 but we might be able to learn.

12 MEMBER THOMADSEN: No.

13 MEMBER VETTER: We can't?

14 MEMBER THOMADSEN: You cannot. And that
15 is thanks to Congress. You cannot get that
16 information. And the hospital cannot give it to you
17 because of confidential peer review. And the reason
18 for that is it's felt that if they don't close the
19 possibility that word and details can get out, that
20 people won't be so forthcoming in freely talking about
21 what happens during the event for the root cause
22 analysis team to be able to do their work.

23 You say, well, they don't have to pass the
24 names, but chances are if you have an event at an
25 institution and you describe what goes on and

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1 physicians talk, you can figure out who is involved.

2 So, instead, to allow the root cause
3 analysis teams to do their work, Congress has said
4 this is all closed and the hospital cannot share that
5 information.

6 It's made a real problem for compliance
7 with the Joint Commission. The Joint Commission has
8 found compliance with a requirement for reporting the
9 sentinel events is very poor.

10 CHAIRMAN MALMUD: Thank you.

11 The effectiveness of double checking is
12 probably the most effective technique, right, when you
13 have two individuals with the same responsibility and
14 one --

15 MEMBER NAG: No.

16 CHAIRMAN MALMUD: -- must check and the
17 other must check off at the same time?

18 MEMBER THOMADSEN: It depends how you've
19 done that. There have been studies that have shown
20 this, too. For example, if you have a form the person
21 checking has to fill in, you need to have two blanks
22 for everything that goes on that form: one blank for
23 what they find and one blank for what they expect to
24 find. That is, you have to write down what you expect
25 as far as dose, for example, and what you actually see

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1 on the plan. If you don't do that, it's too easy just
2 to write down what you expect and not actually see
3 that there is a difference.

4 Also, if the person reviewing checks a box
5 and says, "I've checked the dose," that has almost no
6 value as far as a second review. I mean, there is a
7 great deal of science that goes into sculpting this
8 type of quality management.

9 CHAIRMAN MALMUD: Dr. Fisher?

10 MEMBER FISHER: If one person knows that
11 another person will be checking his results, that
12 person is more highly motivated to be careful in the
13 first analysis.

14 MEMBER THOMADSEN: That is true.

15 MEMBER FISHER: Thank you.

16 CHAIRMAN MALMUD: Dr. Nag?

17 MEMBER NAG: Again, this is a personal
18 observation from practical experience. What I have
19 found is that many of the so-called operator errors or
20 errors occur under pressure when you are trying to do
21 something quickly, which usually happens when a
22 patient is on the table when you are about to give the
23 treatment.

24 And what I have found is if you had a
25 dummy treatment plan already done where you had

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1 something similar for the plan and then you are then
2 doing another plan, which would be altered because of
3 circumstances on the table and then you check on your
4 original plan and if it's not too far, then the
5 chances of having a big error are small.

6 So there are errors and errors. You can
7 have small errors of one percent, two percent, which
8 are not clinically relevant to the patient and not
9 helpful. And you can have a big error. And usually
10 big errors tend to occur when you are in a rush or you
11 have nothing to compare it against. And that would
12 always include to have a backup plan ready or a dummy
13 plan similar to what you are going to do.

14 So, I mean, if we can get some word out if
15 my portion is we do that to the people, but if we can
16 from ACMUI have something like that, that would be
17 helpful to the community.

18 CHAIRMAN MALMUD: Thank you.

19 MEMBER GILLEY: Debbie Gilley,

20 You didn't consider the work environment
21 in your root cause analysis or is it covered under
22 another name?

23 MEMBER THOMADSEN: That was covered under
24 environment.

25 MEMBER GILLEY: That's environment?

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1 MEMBER THOMADSEN: Just environment.
2 Certainly that is very important.

3 MEMBER GILLEY: There is a cooperative
4 spirit amongst physicians, therapist, dosimetrists if
5 this is very important calling through those things.

6 CHAIRMAN MALMUD: Thank you.

7 If we may, then, we will go on to the next
8 item on the agenda, which is Angela McIntosh,
9 "Potential Revision to AO Criteria." It's Angela and
10 staff.

11 MS. TULL: Actually, I have a revised
12 agenda. You may have one in your binder to have all
13 of the names of everyone and the correct times.

14 CHAIRMAN MALMUD: That includes P.
15 Lanzisera and S. Gabriel.

16 8. POTENTIAL REVISION TO AO CRITERIA

17 MS. McINTOSH: Good afternoon. Our
18 presentation is on the future revision to the abnormal
19 occurrence criteria. Let's begin with a definition of
20 what an abnormal occurrence is. It is an unscheduled
21 incident or event that the NRC determines to be
22 significant from the standpoint of public health and
23 safety.

24 The purpose of reporting abnormal
25 occurrences is to keep our stakeholders informed that

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1 they are occurring, our stakeholders being mainly the
2 U.S. Congress and the general public, such as
3 industry, well, you know, industry and the general
4 public, I should say.

5 And abnormal occurrence reporting is
6 required. It's a law. It's not something that's done
7 arbitrarily. We do have to report these things in
8 accordance with the Federal Reports Elimination Sunset
9 Act of 1995.

10 We recently revised the abnormal
11 occurrence criteria. Back in October of 2006, we
12 published the revised criteria in the Federal
13 Register. We revised the criteria for two main
14 purposes, the first being to make sure that the
15 criteria are consistent with our strategic plan for
16 fiscal years 2004 to 2009 but also to make the
17 criteria consistent with the 2005 NRC rulemaking on 10
18 CFR Part 35.

19 Now, to explain briefly what the current
20 criteria are, what we have here on the slide, on the
21 following slides, are redline strikeouts to show you
22 what the changes were, but these are the current
23 criteria.

24 So right there you see that there was a
25 change to the dose to the gonads, that first criterion

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1 equal to or greater than 100 rad to a major portion of
2 the bone marrow, et cetera, or greater than 250 rad or
3 2.5 gray to the gonads or -- all these emphases are
4 mine -- equal to or greater than 1,000 rad to any
5 other organ or tissue. So either one of those
6 criterion plus either A or B would make an event
7 become an abnormal occurrence.

8 Now, the process to revise the abnormal
9 occurrence criteria is similar to rulemaking. We have
10 to submit the criteria for public comment and get the
11 criteria published in the Federal Register. So in
12 terms of the resources that it takes for us to put out
13 new abnormal occurrence, it's similar to a rulemaking.

14 So, in other words, it's a significant
15 undertaking to change the abnormal occurrence
16 criteria. That's one of the reasons why we wanted to
17 bring the proposed revision to you to get ACMUI's
18 input and possible recommendations about what we are
19 proposing because it is a pretty significant resource
20 impact for us to change these criteria.

21 With that --

22 MS. GABRIEL: I'm Sandy Gabriel from
23 Region I. And I am going to briefly talk about an
24 informal review that Region I staff recently performed
25 to determined if all brachytherapy events meeting the

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1 abnormal occurrence criteria are expected to result in
2 significant adverse health effects to the patients.

3 We went through and met reports of
4 brachytherapy medical events for fiscal year 2007 as
5 well as the draft of the 2007 abnormal occurrence
6 reports to Congress.

7 We identified a number of events that
8 appeared to meet the abnormal occurrence criteria,
9 whether or not they were actually reported as AOs, for
10 which the medical consultant concluded that no
11 significant adverse health effect is expected.

12 We also identified some similar events for
13 which there was no medical consultant. These were
14 Agreement State events where a medical consultant
15 wasn't required. That might similarly result in the
16 same conclusion of no significant health effect.

17 This slide shows four events in which
18 permanent prostate implants were displaced from the
19 intended position. All four involved an underdose to
20 the treatment site.

21 And it should be noted that underdoses are
22 not reportable as abnormal occurrences. But because
23 the implants were displaced, there was an overdose to
24 unintended tissue considered to be a wrong treatment
25 site, which would meet the second criteria that Angela

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1 presented a minute ago.

2 I was the inspector for the third event on
3 this list: The New Jersey event. And in this case, a
4 medical consultant did review the case and concluded
5 that no significant adverse health effect is expected.

6 The other three cases represent similar
7 circumstances.

8 The next slide shows four additional
9 events in which temporary implants this time, rather
10 than permanent, were displaced from the intended
11 position. The first on the list was a tandem and
12 ovoid manual brachytherapy treatment. And the three
13 remaining items on the list were HDR treatments.

14 Again, all events involved an underdose to
15 the treatment site as well as an underdose to
16 unintended tissue, which would be considered the wrong
17 treatment site.

18 I was the inspector for the Virginia event
19 shown at the top of this slide. And in this case,
20 which was a tandem and ovoid treatment, the sources in
21 the two ovoid applicators were accurately positioned.

22 However, the tandem insert that was used was four
23 centimeters too short.

24 So the tandem sources were displaced by
25 four centimeters. This caused an underdose to the

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1 cervix, which was a treatment site, and overdoses to
2 very small volumes of adjacent tissue. Again, a
3 medical consultant reviewed this case and concluded
4 that no significant adverse health effect is expected.

5 The next slide shows two additional types
6 of events that may not result in significant adverse
7 health effects. The first is an HDR treatment with
8 fractionation different than was intended. And the
9 second is a liver microsphere treatment that resulted
10 in inadvertent dose to the patient's gallbladder.

11 Now, Penny from Region I is going to speak
12 about possible revisions to the AO criteria.

13 MS. LANZISERA: As Sandy just noted, for
14 many of the brachytherapy cases, the NRC medical
15 consultant concluded that no significant adverse
16 health effects occurred.

17 So the following questions came to mind,
18 and they are represented here. Should the NRC
19 criteria focus on significant health effects only?
20 Should reporting for wrong radiopharmaceutical, wrong
21 root, wrong treatment site, or noted on individual
22 source be removed from the current reporting criteria?

23 So based on this review drafted for
24 discussion today that are summarized at the end of the
25 presentation with the actual language along with the

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1 current AO criteria, the first option that we have
2 here, "Remove the organ and tissue dose criteria and
3 introduce similar concepts," the concept that the dose
4 that occurred is unintended is the first concept
5 introduced.

6 Additionally, we have permanent functional
7 damage or significant adverse health effects
8 represented in the --

9 (Whereupon, the foregoing matter went off the record
10 briefly.)

11 MS. LANZISERA: Again, the permanent
12 function, damage, or significant adverse health effect
13 is added. And this damage would be damage that
14 wouldn't have been expected from the treatment
15 regimen.

16 And what we were thinking here is that
17 this would include the entire patient treatment,
18 brachytherapy along with external beam and any other
19 component of the treatment.

20 The second option retains the 1,000 rad
21 organ tissue dose that is in the current AO criteria
22 and adds the new concept that links this 1,000 rad to
23 the doses greater than the dose expected during the
24 treatment regimen and is done as the patient's entire
25 treatment, which means for the external beam as well.

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1 The third option is similar to option 2
2 but contains also the concept of the 50 percent
3 greater than described as in the current abnormal
4 occurrence criteria.

5 And then the fourth option takes the
6 language for abnormal occurrence from the Federal
7 Register notice, which is "a significant impact on
8 patient health that is likely to generate high public
9 interest," and links that to that this significance is
10 determined by an NRC consultant physician.

11 All of the options provided lead to the
12 concepts of the wrong root, wrong treatment, wrong
13 pharmaceutical. Again, you had that one in your
14 enclosures.

15 CHAIRMAN MALMUD: All right. Does that
16 complete your --

17 MS. LANZISERA: Yes.

18 CHAIRMAN MALMUD: Thank you,

19 Discussion? Dr. Vetter?

20 MEMBER VETTER: Angela, you said that this
21 will involve a lot of effort?

22 MS. McINTOSH: Yes.

23 MEMBER VETTER: And how many events are we
24 talking about affecting here? How many fewer events?
25 If we made one of these changes, how many fewer

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1 abnormal occurrences would there have been in this
2 past year?

3 MS. McINTOSH: Probably would have dropped
4 the number near to zero if not zero.

5 MS. LANZISERA: You'd still have your
6 abnormal occurrence ones for the embryo fetus for
7 those types of events, but all of the prostate ones
8 that are current that are in the current one would go
9 away.

10 MEMBER VETTER: So you think it's worth
11 making the change?

12 MS. McINTOSH: We think that it would.

13 MS. GABRIEL: Yes.

14 MS. McINTOSH: In a word, yes.

15 MR. LEWIS: Part of the problem I think is
16 that in the rest of the agency, where all the abnormal
17 occurrences result in inadvertent exposure, it is a
18 really big deal to Congress. Our definition of
19 medical sweeps in a lot of things that maybe Congress
20 doesn't need to know about and when they tell us, they
21 will tell us.

22 But backing off to put these events in the
23 same tier as the other abnormal occurrences that
24 happen in the agency is really unfair.

25 CHAIRMAN MALMUD: Debbie Gilley?

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1 MEMBER GILLEY: Yes. I noticed that you
2 used consulting physicians to make the determination
3 of the medical impact to the patient. Not all
4 Agreement States do that. Is that a standard for NRC
5 to always use a consulting medical physician?

6 MS. LANZISERA: Yes. It's part of our
7 policy that we offer any medical --

8 MS. GABRIEL: In certain circumstances.

9 MEMBER GILLEY: So you do have some
10 flexibility as to when you would call a physician in
11 to give an opinion of whether or not there are adverse
12 effects to the patient?

13 MS. GABRIEL: We always have the option to
14 do it. And our procedures dictate that in certain
15 circumstances we are required to do it.

16 MEMBER GILLEY: Okay.

17 CHAIRMAN MALMUD: There's another
18 question.

19 MEMBER NAG: I think it definitely is
20 important to have the medical consultant's opinion
21 because I have been a medical consultant on many of
22 these cases. And many of them are from a medical
23 standpoint very insignificant.

24 Legally yes, they are errors or they are
25 abnormal events or medical events, but they are not of

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1 any consequence to the patient, especially these
2 patients would get the external beam.

3 Many of that area would have to radiate
4 much more than that just from that inner beam portion.

5 They directly proportionate a little more dose to
6 that area, which is technically a medical event but to
7 going to affect the patient.

8 So I think it is very important that we
9 separate out things that are going to be a flat thing
10 that the Congress and others need to know about, which
11 is others that really report it and which is important
12 to improve our performance but not necessarily needed
13 to let the entire population be fearful of it.

14 CHAIRMAN MALMUD: Dr. Thomadsen?

15 MEMBER THOMADSEN: Thomadsen.

16 I have my doubts about much of the data
17 upon which you are basing these recommendations. For
18 example, in Kansas, the event for a MammoSite, the
19 implant was just placed 2 centimeters, resulting in
20 100 gray to an unintended site.

21 I've seen many of these accidents. And
22 they actually do have considerable effect on the
23 patient. Particularly in that case, at best, I would
24 have a considerable amount of fat necrosis on the side
25 that was overdosed.

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1 And while you don't consider underdose an
2 event, you have half of the target volume receiving
3 essentially nothing therapeutic, which true for a
4 breast case, probably for a MammoSite case, in
5 particular, the women may not have needed radiation in
6 the first place. But if we assume that we are giving
7 radiation for some reason, underdoses are deadly.

8 In looking at some of the other ones, the
9 medical consultant may have been privy to particular
10 information, but their estimation of the biological
11 effect of the patients are certainly understated.

12 If that is not the case, if that is not
13 the case, then certainly we should along with this
14 change issue a guidance that quality management is no
15 longer important in the medical use of radionuclides
16 since none of these seem to imply that what we do
17 makes any difference whatsoever would simply our
18 tasks as well.

19 CHAIRMAN MALMUD: Well, that's a
20 stimulating statement.

21 (Laughter.)

22 CHAIRMAN MALMUD: Who wishes to respond to
23 it? Mr. Lieto?

24 MEMBER LIETO: What we're talking about
25 here is sort of a special category of medical events.

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1 The medical event is still going to get reported.
2 You know, I am not going to question the judgment of
3 the medical consultant in these ten events, but I am
4 going to just assume that based on their judgment, I
5 support what NRC staff is trying to do here.

6 You know, I am going to look to my
7 colleague in the corner over here, Dr. Suleiman, in
8 that I know FDA has sort of a two-tiered reporting
9 level for medical device problems, anything that
10 causes contoured effect or unexpected effect to a
11 patient. And then there is sort of the -- I don't
12 know the name right off the hand.

13 MEMBER SULEIMAN: One is adverse event,
14 and one is serious adverse event.

15 MEMBER LIETO: Okay.

16 MEMBER SULEIMAN: Seriously basically is
17 potentially life-threatening or whatever. It doesn't
18 define it any more clearly than that.

19 MEMBER LIETO: And I think that is kind of
20 what is being attempted here, is to try to come up
21 with what we report to the Congress and the general
22 public in the Federal Register shouldn't be these
23 events that are maybe below the serious adverse level
24 and only not that -- I mean, it is still going to be
25 reported.

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1 And they still may be addressed by a
2 committee such as ourselves or whatever, but if we are
3 going to take this to Congress, we obviously are
4 indicating these are really, really bad things or
5 undesirable things and should be sort of at the second
6 level of reporting.

7 And maybe what we need to do is come up
8 with addressing along that line. I think that is what
9 these thresholds are attempting to achieve.

10 My concern is only that some of these are
11 very soft terminology, like "expected" and "unlikely."

12 I don't know if we want anything more specific than
13 that, but I support the staff's intent to really only
14 present the events that are determined to be of
15 significant adverse effect.

16 MEMBER SULEIMAN: I'm conflicted. I defer
17 to the oncologists on the Committee because I am
18 surrounded by oncologists at the agency. And my
19 perspective has changed because some of these products
20 are used for cancer patients. Some of them are used
21 for humanitarian or refractory purposes.

22 That means basically that these patients
23 are extremely ill and don't have a very long life
24 expectancy. And so treatment of that cancer may
25 require some skill. And medicine, in some cases, it's

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1 less the science and more the art.

2 So where you draw the line in some of
3 these quantitative, you know, 50 percent, 25 percent,
4 I am conflicted with the term "error." I think there
5 is a baseline uncertainty. You just have a certain
6 level of imprecision in delivering the therapeutic
7 dose. I think that's just the state of the practice.

8 You know, is it one percent? Is it five
9 percent? Is it ten percent? We tend to look at the
10 numbers and think they are all the same. So I think
11 it would require a little bit more thinking through.

12 I can't give you a straight answer or an
13 opinion, but, I mean, I would be very, very hesitant
14 to call a dose that a prescribing physician decided,
15 you know, "This patient is pretty ill. Let's giving
16 him something a little bit" -- you're not sure what
17 amount of dose you want to prescribe.

18 And some of these are new procedures. So
19 you're still learning. So I would be very, very
20 careful about one quantitative change fits all sizes.

21 CHAIRMAN MALMUD: Dr. Welsh?

22 MEMBER WELSH: I'd like to look at this
23 from a big picture perspective and ask, what is the
24 goal of possibly changing things here or revising
25 things? And one answer that I heard posed was that we

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1 should be asking, what do Congress and stakeholders
2 really want to be informed about? How important are
3 these things?

4 I don't want to question the judgment of
5 the medical consultant, but, as Dr. Thomadsen pointed
6 out, there could be some effects. And you would
7 expect some effects from the cases that are listed
8 here. But are they defined as significant adverse
9 effects?

10 These gentlemen who have received dose to
11 the penile bulb would probably have erectile
12 dysfunction. Does Congress need to know about that?
13 Probably not.

14 So the important point is, what is the
15 definition of an adverse effect? And how can we make
16 sure that we are quantitative in defining this so that
17 we can be confident that things that don't have to go
18 to Congress don't wind up going there?

19 CHAIRMAN MALMUD: Dr. Nag?

20 MEMBER NAG: I would also like to state
21 that there is a wide range of diverse opinion in
22 different treatments. And let's say if you are giving
23 a drug by weight and you are allowing 20-30 percent
24 difference or you are giving medication that absorbs
25 at different levels in different parts of the body and

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1 then you are comparing that with brachytherapy and you
2 are holding brachytherapy to such strength that if it
3 is 21 percent more to an area that you are not even
4 sure of. You are not sure where the packet is.

5 And you are arbitrarily saying, "This is
6 the target, and you are getting 21 percent more
7 through this area." And that is an abnormal event,
8 and you call that an abnormal occurrence. Then you
9 are really holding to very inconsistent standards.

10 I think that at least having a physician
11 making that determination is helpful, that was this
12 error or was this deviation of significant proportion
13 that the public at large needs to know about.

14 I know in chemotherapy, very often if you
15 feel the patient is sick, you go down by 50 percent or
16 70 percent of the dose. And that is even advisable;
17 whereas, in brachytherapy, the whole thing is very
18 strict.

19 Just because it is under the definition of
20 a medical event, that does not necessarily mean that
21 there has to be a big alert. Yes, we need to know
22 about this. Yes, we need to see how we can collect
23 it.

24 CHAIRMAN MALMUD: Dr. Eggli?

25 MEMBER EGGLI: My comment sort of sits at

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1 a 50,000-foot level because I don't know enough about
2 this to talk in detail. But usually that doesn't stop
3 me.

4 It seems that the intent here, the key
5 part of this is the expected-to-result permanent
6 functional damage and that the intent is to reduce the
7 reporting of events that don't have severe
8 consequences.

9 Now, you can take the minimalist approach
10 and just use that, but then nobody really knows where
11 to start thinking about is this causing damage or what
12 should be the threshold events that I might want to
13 evaluate.

14 So from that point of view, I actually
15 like option 3 best because everything else is trumped
16 by what now is to be in option 3. If it doesn't hit
17 that threshold, since there is "and" there, if it
18 doesn't hit that threshold, it is not reportable but
19 having in the other items sort of list what other
20 things you might want to think about as maybe pushing
21 you to the threshold where you might have significant
22 damage in part 2.B.

23 So if you take option 1, you know, why is
24 101 gray to the bone marrow or 2.5 gray to the gonads
25 more important to leave in as a specific reference

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1 than 10 gray to other organs or tissues or 50 percent
2 over dose prescribed? You know, what makes one of
3 these criteria more important to sort of raise or
4 sensitize people with?

5 So it makes sense to me that if the 2.B
6 threshold trumps everything else, which is that there
7 is no other tissue damage, then what you are doing
8 here is listening conditions that you want people to
9 think about as maybe causing significant damage and
10 maybe ought to be triggers for evaluation.

11 So I would use option 3. If your point
12 here was to get advice, that is one person's opinion.

13 MEMBER WELSH: May I comment on that?

14 CHAIRMAN MALMUD: Please do.

15 MEMBER WELSH: When I was bringing up the
16 point earlier about quantitation, it is sort of a
17 rhetorical question because significant injury -- is
18 that 50 percent risk of injury, 100 percent? There's
19 no definition.

20 If we had to make up a definition, I think
21 we would all come up with something slightly different
22 in terms of what number of sieverts or gray would
23 reach the 50 percent threshold. That's why I like
24 option 4, because it's the only one that's not put in
25 numbers.

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1 And if we are going to stick to something
2 quantitative and defined, it is going to be difficult.

3 Death is easily defined. And number two might be a
4 little bit more subjective, but still it avoids the
5 issues of numbers.

6 CHAIRMAN MALMUD: Thank you.

7 Dr. Eggli?

8 MEMBER EGGLI: What I don't like in option
9 4 is who is deciding what is public interest? Is it
10 Geraldo or Oprah? You know, who is deciding what is
11 of significant public interest here? That is going to
12 the sensationalists are going to find everything of
13 significant public interest. And what is the
14 definition of significant public interest?

15 So that part of number 4 I don't like at
16 all, actually.

17 CHAIRMAN MALMUD: Mr. Lieto?

18 MEMBER LIETO: As a compromise, could we
19 move 2.B in option 3 into 2 of option 4? Would that
20 make sense?

21 MEMBER THOMADSEN: Actually, if you do
22 that, you don't need option 1 in number 4 because I
23 think 1, the death, could be considered a permanent
24 function.

25 (Laughter.)

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1 MEMBER LIETO: I would accept that
2 modification.

3 MEMBER GILLEY: Definitions of these two
4 to assist in determining whether there have been
5 significant adverse health effects. Is NRC prepared
6 to do a definition for those things?

7 MEMBER VETTER: Coming from the physics
8 side that would have to measure things, I would vote
9 for option 3. The option 4 is just so subjective for
10 me it's hard to get my hands around it.

11 MR. LEWIS: What I think is not subjective
12 about option 4 is in the opinion of the medical
13 consultant. So it always comes back to that one
14 person's opinion is what we would decide to send down.

15 And if it's option 3, number 2.B, it
16 doesn't have that. So I think it also answers
17 Debbie's question. It's a medical consultant's
18 opinion that was the defining criteria in that option.

19 MEMBER GILLEY: Is it then implied that we
20 will need to have a medical consultant every time
21 there is a medical event to give a recommendation?
22 Because that is additional --

23 MR. LEWIS: Significant.

24 CHAIRMAN MALMUD: Dr. Fisher?

25 MEMBER FISHER: Darrel Fisher.

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1 From a patient perspective, there really
2 are only two considerations that are important, I
3 think. One, was the proper treatment delivered that
4 would result in a beneficial therapeutic effect? And,
5 two, was an improper delivery of radiation avoided
6 that could result in some permanent dysfunction or
7 adverse effect? Whether it's 990 or 1,050 is
8 irrelevant to the patient. I mean, there is no magic
9 number that says above 1,000, you have a significant
10 event. Below 1,000, you don't have.

11 And so I think the important concept here
12 would be not so much whether Congress thinks it is a
13 significant event or the news media but, rather, did
14 the patient receive the proper dose to the target
15 tissue? And doses to normal tissues should not have
16 been irradiated, were they avoided? I think it is as
17 simple as that.

18 MS. McINTOSH: Can I respond to that?

19 CHAIRMAN MALMUD: Yes. Angela?

20 MS. McINTOSH: I think we agree that
21 always important is the patient perspective on what
22 has occurred. It's their body. And we should always
23 be sensitive to that. But with these criteria, we are
24 required to report certain things to Congress. And
25 that is built into the whole reason for why we are

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1 doing this.

2 And so the criteria were initially
3 developed from, actually, the reactor side of the
4 house from events that would occur in the reactor
5 realm that Congress might be interested in knowing and
6 the public might be interested in knowing.

7 And the medical materials side of the
8 house has sort of come in after the fact, for lack of
9 a better term, and been sort of retrofitted into
10 something that was created in the reactor realm.

11 And from our perspective, what this has
12 done, it has created a situation where the significant
13 reactor events Congress is aware of, but the
14 commensurate medical events are not really as
15 significant.

16 And so we don't want to ever disregard the
17 importance of keeping the patients involved about
18 their own treatment and issues with their own medical
19 treatment. But we just want to elevate the medical
20 events so that there is an equivalency in significant
21 adverse impact that has happened on the medical side
22 of the house.

23 We currently think that that equivalence
24 just doesn't exist. And so that is what we are trying
25 to correct and not inform Congress of every little --

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1 you know, pardon the expression -- little by
2 comparison, relatively speaking, little medical event
3 so that they are not just inundated with things that
4 really from their standpoint, it just isn't
5 significant.

6 CHAIRMAN MALMUD: Thank you.

7 Dr. Suleiman?

8 MEMBER SULEIMAN: I mean, FDA does have a
9 severe adverse event reporting system. And things
10 sometimes happen out of the ordinary. I think what I
11 do like in the wording of some of these is that, I
12 mean, side effects, some of these medical products
13 have some very serious side effects.

14 And I guess I can reconcile the
15 physician's right to prescribe a dose, even though
16 those prescribed doses may vary a lot. That is
17 tolerable under the practice of medicine.

18 But once they have made up their mind,
19 they are going to deliver such and such amount of
20 activity or whatever. And if something happens where
21 the patient gets much, much more than that, death
22 results or whatever, the purpose of these regs is to
23 sort of identify these outliers.

24 So I think conceptually you are right.
25 The problem is how do you calibrate the abnormal

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1 occurrences from the medical events from a single
2 case-by-case situation as medicine is practiced from
3 forgetting the genesis but the lack of thing that is
4 going to -- you know, it's something that would have
5 an impact on a large population in the immediate area.

6 So here we want, the FDA wants to see the
7 reports because there may be a trend developing here
8 that is going to affect an awful lot of patients using
9 something. So if there is a protocol or there is a
10 device malfunction or there is a problem with a
11 radioactive drug, you need to get -- I would think
12 that would be picked up more on the medical event
13 side, rather than the abnormal occurrence side.

14 CHAIRMAN MALMUD: Dr. Thomadsen?

15 MEMBER THOMADSEN: Out of ignorance
16 because I don't really follow them, what are some of
17 the reactor events? What is a typical reactor event
18 that is reported? And how many people die from them?

19 MS. McINTOSH: I have no idea. Do you
20 have that? I don't have the --

21 MS. LANZISERA: I don't believe there were
22 any for this year, but the top part of the language,
23 the 100 rad, the major forces of bone marrow, that
24 also would be typical to any of the reactor
25 facilities. The 250 exchange, that would be 100 rad

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1 for the reactor facilities.

2 MS. FLANNERY: Dr. Malmud?

3 CHAIRMAN MALMUD: Yes?

4 MS. FLANNERY: There is somebody back here
5 who probably could answer that specific question.

6 MS. BUSH-GODDARD: My name is Stephanie
7 Bush-Goddard. I am the Chief of the Health Effects
8 Branch of the Office of Research. We actually are the
9 office that lead the AO criteria.

10 In the last five years, about 90 percent
11 of the events in the abnormal occurrence report have
12 been medical events. The last reactor events were
13 actually there were fuel events, a possible
14 criticality or something like that.

15 But in the last five years, we have had no
16 more than about five reactor events. And each year we
17 average about 11 to 13 medical events in the abnormal
18 occurrence report.

19 CHAIRMAN MALMUD: Thank you for that
20 clarification.

21 Dr. Vetter?

22 MEMBER VETTER: Yes. Could we go back
23 again? What is the intention of notifying Congress
24 and the general public about these events?

25 MS. McINTOSH: The intent is to make them

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1 aware of events that the AO reporting requirement is a
2 law required of us to report to Congress events that
3 NRC considers significant from the standpoint of
4 public health and safety.

5 MEMBER VETTER: So it's quite subjective?

6 MS. McINTOSH: There is some subjectivity
7 to that, yes, what we consider significant. And that
8 I think is probably more easily defined on the reactor
9 side of the house -- correct me if I am wrong -- than
10 it is on the medical side of things, than it is on the
11 medical application of radioactive material.

12 CHAIRMAN MALMUD: Dr. Nag?

13 MEMBER NAG: I would like to ask a
14 question here. In most of the other reactors and so
15 forth, you are not expecting to give radiation to the
16 public. And, therefore, you have a limit set that we
17 selected more than somewhat to the Board and so forth.

18 Here your objective is to give some
19 radiation to that person. But I do not see anything
20 here where if you did not give that radiation, that is
21 an abnormal effect.

22 I would have thought that severe
23 underdosing would be an abnormal effect. That is, if
24 the tumor went to get 110 ray and it never got
25 anything, it didn't get anything, that would have been

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1 an abnormal event. But nothing is listed on the
2 underdosing side.

3 MS. McINTOSH: The first criterion that
4 must be met is that the event must be a medical event.

5 And then after it is a medical event, we look at how
6 much the patient was given that was not expected to be
7 given. So that does rule out the underdosing, but the
8 underdosing we feel is addressed. And, in fact, it is
9 still a medical event.

10 MEMBER NAG: It is a medical event, but it
11 will not be an abnormal occurrence.

12 MS. McINTOSH: No.

13 MEMBER NAG: And if, for example, there
14 was an LMA or whatever, you are penalizing. What I'm
15 worried about is because you are penalizing someone
16 for a possible mistake in the upper side, the
17 physician will try to lower the dose so that they
18 don't make any -- you know, if they make any mistake,
19 it will be on the lower side and not on the upper
20 side.

21 And that is something I have seen in
22 hospitals that physicians know that if they make an
23 error and they gave a little too much, they would have
24 a side effect cause on the face, then they would be
25 either sued or, you know, they would have a medical

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1 event.

2 So that was the intent to bite down on the
3 dose. And if you bite down on the dose and the
4 repellents or the tumor did not get cured, you do not
5 have any penalty for that. That's where I'm getting
6 at.

7 CHAIRMAN MALMUD: I think that Dr. Welsh
8 was next, and then you are next after that.

9 MEMBER WELSH: I would like to just go
10 back to Dr. Vetter's question, which I think is the
11 key question of this whole discussion here. What does
12 Congress and what do we feel we really have to report?

13 It would seem to me that you would want to
14 reserve this abnormal occurrence definition to
15 something that is very severe, perhaps that causes
16 death or is life-threatening.

17 If 90 percent of AOs are in the medical
18 field -- and I doubt that many people die -- it seems
19 like we are grossly over-represented here. And,
20 therefore, we should be choosing the option that is
21 most stringent or saying that when that results in
22 death or is life-threatening. And I think that that
23 would be the most practical solution to this dilemma
24 that we're facing at the table here.

25 CHAIRMAN MALMUD: Excuse me. Are you

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1 saying that results in death or life-threatening in
2 the opinion of a consultant physician?

3 MEMBER WELSH: If that is what is required
4 by NRC to have that consultant make that opinion, yes,
5 that would be --

6 CHAIRMAN MALMUD: Are you suggesting,
7 then, option 4 with one change? And that is that a
8 phrase referring to "likely to generate high public
9 interest" be dropped?

10 MEMBER WELSH: Correct.

11 CHAIRMAN MALMUD: That's option 4, part 1.
12 Part 2, it says, "significant impact on patient
13 health as determined by an NRC consultant physician."

14 MEMBER WELSH: Is that the NRC?

15 CHAIRMAN MALMUD: Well, by a consultant
16 physician? By a consultant physician.

17 MEMBER FISHER: A regulatory consultant
18 physician.

19 CHAIRMAN MALMUD: I beg your pardon?

20 MEMBER FISHER: A designated regulatory
21 consultant physician. It's not just any consultant.

22 CHAIRMAN MALMUD: Well, then it's an
23 NRC-designated consultant, NRC or Agreement
24 State-designated consultant physician, NRC or
25 Agreement State-designated consultant physician.

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1 Let's try that wording, if we may. And I think,
2 having listened to this discussion, that that might
3 meet the needs of most, if not all, of your concerns.

4 Dr. Nag?

5 MEMBER NAG: Just a slight modification
6 from what you have stated.

7 CHAIRMAN MALMUD: Yes?

8 MEMBER NAG: I would say option 4, which
9 is what you said, one.

10 CHAIRMAN MALMUD: Yes.

11 MEMBER NAG: And then it's option 3, 2.B.
12 And that would be one other thing because otherwise a
13 significant impact on patient health is not that
14 clear, whether here the radiation exposure would
15 result in permanent functional damage or significant
16 health effects that would not have been expected.
17 That's a little more clear, you know, I would say,
18 number one, option for number 4 plus option 3, number
19 2.B. It would be really clear or more clear than what
20 you have now.

21 CHAIRMAN MALMUD: Well, may I just
22 question you about that? When you get informed
23 consent from a patient prior to treating, is it not
24 common to tell the patient that the risks include some
25 of these terrible things, such as radiation to the

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1 bladder, impotence, et cetera, et cetera?

2 And, therefore, when you say "would not
3 have been expected," they were in a sense expected
4 because they were part of the informed consent.

5 MEMBER NAG: Well, not really. I mean,
6 the reality is the next day you may have bladder
7 damage and so forth. That is more risk, but you don't
8 really expect that from a regular treatment.

9 But that is where I think the medical
10 objection was coming to be, that in the normal course
11 of events, would this treatment have for us that
12 damage?

13 You know, quite simply, the tumor is in
14 the rectal- vaginal septum, between the rectum and the
15 vagina. If you have damage to the rectum in that
16 stage, that stage almost I wouldn't say is expected,
17 but there is a high likelihood. And I don't think a
18 physician would say that is unexpected.

19 If the tumor was somewhere else and it
20 resulted in damage to the rectum, you would have upset
21 that in your consent. You know, that is not something
22 you expect to happen. And that would be an incident
23 that is an unexpected event.

24 CHAIRMAN MALMUD: Well, then, if I may
25 again, what about if we do a merger of these two,

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1 namely option 4, part 1, no change; part 2, a
2 significant impact on patient health? That would
3 result in permanent functional damage or a significant
4 adverse health effect as determined by --

5 MEMBER NAG: Yes.

6 CHAIRMAN MALMUD: -- the NRC consultant
7 physician?

8 MEMBER NAG: Yes.

9 CHAIRMAN MALMUD: How's that?

10 MEMBER NAG: That's fine. I mean, that is
11 similar to what I said.

12 CHAIRMAN MALMUD: Yes, yes.

13 MEMBER NAG: I fully agree with you.

14 CHAIRMAN MALMUD: I am just trying to
15 think of both sides of it, namely protecting the
16 patient, at the same time not putting the radiation
17 oncologist at undue risk for having made an error that
18 was one of the errors that might occur.

19 Dr. Suleiman?

20 MEMBER SULEIMAN: Clarification. If the
21 NRC is reporting to Congress 11-12 AOs and one or 2
22 reactor ones every couple of years, how has that been
23 received? Is it a problem?

24 MS. McINTOSH: It's not a problem. It's
25 just they're getting information that they have a low

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1 interest in.

2 MEMBER SULEIMAN: I mean, we have hundreds
3 of thousands of these things.

4 MS. McINTOSH: I mean, it's not a problem
5 per se. There's just not really much benefit from
6 reporting these, relatively speaking, low-significance
7 medical events to Congress.

8 CHAIRMAN MALMUD: When they are reported
9 to Congress, then it generates a question from the
10 Commission to us about whether or not we should be
11 tightening the rules because I received that question
12 in a private session.

13 MS. McINTOSH: So that could be a danger
14 that maybe it's creating an artificial concern.

15 CHAIRMAN MALMUD: If we report trivial --
16 nothing that injures any of us personally is trivial.

17 And, therefore, nothing that injures any member of
18 the public is trivial. But if it's a relatively small
19 risk and reporting it to Congress elevates it to the
20 position of something that it is not and, therefore, I
21 think that given the wording that was suggested by --
22 who suggested number 4? -- Dr. Welsh and Dr. Nag,
23 combining that, I think we may have achieved what you
24 are aiming for.

25 Rob Lewis?

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1 MR. LEWIS: I appreciate the Committee's
2 work on this. I think that we have to take it back;
3 in particular, the aspect of high public interest.
4 And I certainly understand the subjectivity related to
5 that, but the NRC's need will probably be framed, at
6 least partially, in terms of high public interest.

7 For example, if a reactor narrowly avoided
8 a meltdown or fuel facility narrowly avoided a
9 criticality event, just by luck, that certainly needs
10 to be reported to Congress. And we have to find a
11 parallel situation in the materials world that needs
12 to be reported to Congress.

13 Nobody was exposed of any dose in those
14 situations. And, in fact, that is the reality, is we
15 are revising the AO criteria because of what happened
16 at a field facility that narrowly avoided a
17 criticality which was not reported to Congress until a
18 year later.

19 CHAIRMAN MALMUD: Yes, but this is a very
20 different world. This is a medical world in which we
21 are discussing sequelae to patients that don't occur
22 often statistically but do occur in the practice of
23 medicine. To report these routinely to Congress is to
24 elevate them to a level of concern that may not be
25 appropriate with regard to making legislation.

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1 MR. LEWIS: I absolutely agree with that
2 and understand what you are saying, but I do think
3 that there needs to be leeway for an issue that will
4 have a high public interest for NRC to tell Congress
5 that we think this is an issue that may have high
6 public interest.

7 It's not the 19 things we have been
8 reporting, but it is something. And we've got to
9 define what that something is.

10 CHAIRMAN MALMUD: Therefore, your feeling
11 is that the phrase "public interest" should somehow
12 remain there?

13 MR. LEWIS: Well, I am just trying to be
14 realistic with the Committee about we can take this
15 feedback, but I think that the group that is working
16 on the issue at NRC is going to have to include that
17 in part of their debate. I know the senior management
18 of NRC is looking for that.

19 CHAIRMAN MALMUD: Thank you for informing
20 us. We have a member of the public, and then I think
21 we have -- oh, you've been waiting longer.

22 (Laughter.)

23 CHAIRMAN MALMUD: You've been waiting
24 longer. Okay.

25 MEMBER GILLEY: I just want to make one

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1 clarification. I've done 10 to 12 medical event
2 investigations as team leader. And in no
3 circumstances when we have had an under-exposure has
4 the patient not been treated adequately.

5 Physicians have always gone back and
6 altered their treatment to get the best possible
7 medical care. I don't want anybody in this audience
8 to leave thinking that that is not happening and we
9 have allowed that as part of their corrective action
10 when such events are occurring.

11 CHAIRMAN MALMUD: Thank you for putting
12 that in the record.

13 We have a member of the public.

14 MS. FAIROBENT: Yes, Lynne Fairobent with
15 AAPM.

16 Dr. Malmud, a couple of things. One, I am
17 concerned a little bit about the language where are
18 mandating NRC or Agreement State-designated consultant
19 physicians. If this wording were to go through, this
20 would have to be a case in every instance.

21 Debbie, what is the compatibility on AOs?

22 MEMBER GILLEY: I think that's a
23 compatibility B.

24 MS. FAIROBENT: That's what I was
25 thinking. And, just to reiterate what Debbie said

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1 earlier, there are many Agreement States that
2 currently do not necessarily bring in a consulting
3 physician for every AO that occurs within their
4 jurisdiction. And they may not have the funds to do
5 so. They may not have the authority to do so in all
6 cases. So I think that needs some consideration.

7 The other thing is having spent over 30
8 years in most of my career in the reactor end, I do
9 think we are sending a wrong signal to Congress. If
10 you take a look at the history of what has gone up in
11 the AOs, medical dominates.

12 And, yet, I would have to take issue with
13 they are not on parallel. And I'm not so sure there
14 is a parallel definition that we can come up with for
15 what is in the reactor or fuel cycle world that is
16 reported to Congress.

17 I do think with the heightened security,
18 the heightened interest in Congress right now on what
19 is happening with medical uses and medical sources
20 from increased controls. Continuing the practice of
21 reporting or dominating the AO reports with medical
22 events may pose unwanted scrutiny and unwanted
23 legislation to come down the road that none of us is
24 looking for.

25 So I just want to throw that balance out

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1 as for both the Committee as well as the staff to
2 consider because it is not as simple as coming up with
3 a one-to-one match in the materials, especially in the
4 medical material sides.

5 CHAIRMAN MALMUD: Thank you.

6 Dr. Thomadsen?

7 MEMBER THOMADSEN: In our proposal there,
8 what would actually trigger a call to the NRC or to
9 the Agreement State? I don't see that it's at all
10 clear what would be considered an incorrect
11 administration, particularly if we assume that you can
12 do all this dose incorrectly and it has no effect.
13 What would be an incorrect administration?

14 CHAIRMAN MALMUD: Well, 100 millicuries of
15 I-131 orally to a woman who is pregnant.

16 MEMBER THOMADSEN: Well, we are leaving
17 out the fetal situation because we have already said
18 that's not under this. That's under a different rule.

19 CHAIRMAN MALMUD: A hundred millicuries --

20 MEMBER THOMADSEN: Well, if you give 100
21 millicuries of iodine to somebody who is expecting a
22 prostate implant, I think that would probably fall.

23 CHAIRMAN MALMUD: What about two patients
24 scheduled the same day: One to receive 10 millicuries
25 for hyperthyroidism, the other to receive 100

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1 millicuries for thyroid cancer, and the doses are
2 switched, they both have last names Johnson?

3 MEMBER THOMADSEN: Would you expect to
4 have any significant impact on the patients?

5 CHAIRMAN MALMUD: Yes. The 100
6 millicuries to a patient with an intact thyroid could
7 result in -- well, definitely will result in wiping
8 out the thyroid but could result in a release of
9 hormone, which would also cause the patient some acute
10 distress.

11 MEMBER THOMADSEN: In that case, you don't
12 need anything before you get to the two there. I
13 would say it is for medical licensees, any
14 administration with significant impact. You don't
15 have to even have any of that stuff.

16 MEMBER WELSH: Can I ask a question?

17 CHAIRMAN MALMUD: Good point.

18 Dr. Welsh?

19 MEMBER WELSH: Maybe I'm misunderstanding
20 something, then. Do these have to be medical events?

21 MS. McINTOSH: Yes.

22 MEMBER WELSH: So that's what it is. It's
23 a medical event that results in. So I think that
24 answers.

25 MEMBER THOMADSEN: How do define a medical

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1 event, then? Are you still keeping the same criteria
2 that you had before?

3 MS. McINTOSH: Yes, 35.3045, yes.

4 MEMBER THOMADSEN: Okay. I thought that
5 was replacing all of that.

6 MS. McINTOSH: No, no, no.

7 MEMBER WELSH: So perhaps we should use
8 the more precise terminology, then, "medical event,"
9 not "results," then. And then there won't be
10 questions like this.

11 CHAIRMAN MALMUD: A medical event, not
12 results in.

13 MEMBER NAG: Do we need death? Because
14 significant impact on the health, I mean, that is
15 already a significant impact. So we probably don't
16 even need death because if you have death, it is a
17 significant impact.

18 MEMBER THOMADSEN: Well, no because you
19 could have a significant impact on a patient's health
20 that does not qualify as a medical --

21 MEMBER NAG: Well, it is a medical event
22 that results in death.

23 MEMBER THOMADSEN: That's why I am saying
24 you need to have that. You need to have that medical
25 event in there.

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1 MEMBER NAG: I'm saying death.

2 MEMBER THOMADSEN: I'm not saying you
3 don't put that in there.

4 MEMBER NAG: I'm saying death.

5 MEMBER THOMADSEN: Death is a medical
6 event.

7 MEMBER NAG: Why do you need death there?

8 MEMBER THOMADSEN: I've said that before.

9 MEMBER SULEIMAN: That is unexpected. I
10 mean, you've got to differentiate between the serious
11 possible anticipated side effects for oncology
12 patients.

13 But I have no trouble recording those
14 numbers. I mean, you're defining it in such a way
15 that these are really problematic. And I think if I'm
16 reading these reports, that's the base for medical
17 practice. I mean, you're seeing some very serious by
18 definition abnormal occurrences. And why should you
19 be afraid of reporting those numbers?

20 I think the numbers are very small if
21 you're only reporting a dozen a year. I mean, do you
22 want to say zero? I think that's an impossible
23 expectation.

24 CHAIRMAN MALMUD: If I may, we don't want
25 to show zero. We want to show that we are monitoring

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1 this. At the same time, we don't want to alert
2 Congress to issues which don't require congressional
3 oversight because they are routine problems dealt with
4 by other methodologies in the practice of medicine.

5 MEMBER VETTER: I'd like to move that we
6 support what is on the board there, that particular
7 option, option 4, as a --

8 CHAIRMAN MALMUD: Dr. Vetter recommends
9 that the proposal read as follows, "A medical event
10 that results in: 1) death, or 2) a significant impact
11 on patient health that would result in permanent
12 functional damage or a significant adverse health
13 effect as determined by an NRC or Agreement
14 State-designated consultant physician."

15 PARTICIPANT: Second.

16 CHAIRMAN MALMUD: It has been moved and
17 seconded. Is there any further discussion of that?

18 MS. TULL: On 2.B, there would actually
19 not have been a second on the normal treatment
20 regimen. Do you want that piece in there or no?

21 MEMBER NAG: Yes.

22 MS. TULL: I mean, put it there and --

23 CHAIRMAN MALMUD: That would not have been
24 expected from the normal treatment regimen.

25 PARTICIPANT: Yes.

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1 MEMBER LIETO: Mr. Chairman? This is
2 Ralph Lieto.

3 That is what you had suggested originally.

4 CHAIRMAN MALMUD: Yes, that's what we had
5 suggested originally. Okay. So that is the motion,
6 which has been seconded, on the floor. Any further
7 discussion of that motion? Dr. Welsh?

8 MEMBER WELSH: Just for Rob Lewis' comment
9 about likely to generate high public interest, I
10 understand and appreciate the concern. But if we
11 would include it in 4, it probably should have been
12 included in 1, 2, and 3 as well. So I would say that
13 unless people feel strongly, I am comfortable with
14 dropping it altogether.

15 CHAIRMAN MALMUD: Mr. Lieto?

16 MEMBER LIETO: I would like to just
17 support what Dr. Welsh said because if you look at the
18 abnormal occurrences reported, the trend that was
19 reported in our Subcommittee report, you would see
20 that there were these numbers that were consistently
21 between 10 to 11 or 5 to 11 events over the last 4
22 years.

23 And, yet, there's been nothing apparently
24 that's coming back regarding those over those past
25 four years of events that have indicated interest by

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1 Congress with those types of events.

2 CHAIRMAN MALMUD: Any further discussion?

3 MEMBER NAG: One other.

4 CHAIRMAN MALMUD: Dr. Nag?

5 MEMBER NAG: I'm wondering whether we can
6 simplify. Actually, I like what you have there, but I
7 wonder whether we can simplify it by just eliminating
8 death because that is redundant. And then if you have
9 death, that is a significant adverse health effect.

10 CHAIRMAN MALMUD: I believe -- I didn't
11 draft this, and this is not my crafting. This is a
12 Committee crafting.

13 MEMBER NAG: Right.

14 CHAIRMAN MALMUD: We have to all take
15 credit for it. I think the death stands out as a
16 terrible outcome which should be highlighted as an
17 issue of grave concern.

18 MEMBER NAG: Yes, right.

19 CHAIRMAN MALMUD: No pun intended. And,
20 therefore, putting it first is appropriate in this
21 situation, I would suggest.

22 Sally?

23 MEMBER SCHWARZ: I'm sorry. I was just
24 stating in terms of the FDA, that death is always
25 stated in adverse reactions.

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1 MEMBER SULEIMAN: Or life-threatening.

2 MEMBER SCHWARZ: Or death first.

3 MEMBER SULEIMAN: What is proposed is what
4 is on that screen?

5 PARTICIPANT: Yes.

6 CHAIRMAN MALMUD: Option 4.

7 MEMBER SULEIMAN: With the corrections?

8 CHAIRMAN MALMUD: With those corrections,
9 which really are an amalgam of several other
10 recommendations that were made. That is the proposal.
11 Let's call the vote. All in favor?

12 (Whereupon, there was a show of hands.)

13 CHAIRMAN MALMUD: Any opposed?

14 (No response.)

15 CHAIRMAN MALMUD: Any abstentions?

16 (Whereupon, there was a show of a hand.)

17 CHAIRMAN MALMUD: One abstentions.

18 Otherwise, all in favor. Thank you.

19 2:45 plus 30. We can take a break. May
20 we take a break before we move on to Dr. Welsh and
21 emerging technology.

22 (Whereupon, the foregoing matter went off the record
23 at 3:12 p.m. and went back on the record
24 at 3:32 p.m.)

25 CHAIRMAN MALMUD: Thank you all. We will

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1 get started now. Dr. Welsh, we will do his
2 presentation on radioiodine label, phospholipid
3 ethers, cancer diagnosis and treatment.

4 DR. WELSH: Thank you, Dr. Malmud and I
5 will be talking to you today about these radioiodine
6 labeled PLEs or phospholipid ethers and diagnosis and
7 treatment. This, I think, is one of the most exciting
8 things that will be coming along in 2008. These
9 phospholipid ethers can be radio-labeled and the
10 investigators has chosen to use radioiodine and are
11 looking at I-125, I-131, I-124 for imaging.

12 The basis for this is the selective
13 retention of these phospholipid ether compounds in
14 malignant tumor cells but not in hyperplasias,
15 inflammation and other benign conditions. Thus far,
16 the investigators have demonstrated selective tumor
17 uptake in all human and rodent tumor models evaluated.

18 It says 30 out of 30. I think they've checked out
19 over 40 now and the concept of the universal oncologic
20 tracer with a magic bullet, this is the closest I've
21 ever seen us come to it.

22 It's not taken up into the brain through
23 an intact blood brain barrier. So you can have brain
24 tumor imaging. It does accumulate in tumors in the
25 brain but not in normal brain tissue.

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1 There's an insignificant renal elimination
2 which means that it doesn't accumulate in the bladder
3 and therefore you can visualize the prostate or
4 prostate bed. Initial human investigations have
5 confirmed that what is seen in rodents seems to be
6 happening in humans as well as far as the imaging
7 goes.

8 So how does it work? Well, nobody knows.

9 It's one of those kinds of things that in theory did
10 not receive the grub (phonetic) development as far as
11 I understand. The phenomenon is that phospholipid
12 ethers accumulate in malignant cells but not normal
13 cells. Phospholipid ethers integrated into the cell
14 membrane are degraded by phospholipase. Phospholipase
15 D may be the principal one in this particular case and
16 normal cells metabolize these products and clear them
17 from the cells.

18 Something goes wrong in malignant cell
19 membrane metabolism such that these phospholipases do
20 not degrade phospholipid ether compounds and there's
21 low, there is no metabolism of the parent compound and
22 these small molecules are retained in the cell
23 membrane.

24 So here's a brief summary of some of the
25 accumulation studies. All of these are tumor

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1 xenografts of various histologies and they do seem to
2 accumulate and are retained in the tumor cells.

3 On the other hand down at the bottom,
4 there were a couple of benign tumors that did not
5 accumulate the phospholipid ether compounds. So it
6 seems to be selective in malignant cells. Somewhere
7 along the process of malignant transformation in
8 addition to what we learned in the textbooks about
9 molecular changes and genetic alternations, also
10 something is going on with perhaps phospholipase D so
11 that malignant cells cannot metabolize phospholipid
12 ethers properly.

13 A company has been formed and it's called
14 Celectar and they have chosen a specific phospholipid
15 ether analog and they call it the CLR1404. They have
16 tested hundreds of these phospholipid ethers and found
17 that short chain ethers with maybe five to eight
18 carbons are metabolized in normal cells but longer
19 chain compounds, 12 to 15 or 18 carbons, are not
20 easily metabolized. That's where this 1404 is found
21 to be the one that is retained longest in the normal
22 cells, can be labeled with iodine and some preliminary
23 results have been published.

24 Here's an example of imaging and they used
25 I-125 here. You'll see that on Day One it does seem

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1 to accumulate in the tumor, but the interesting thing
2 is that over time moving from left to right you can
3 see that it is washed out through the remainder of the
4 body and now is selectively accumulated and retained
5 in this adrenal tumor model.

6 Here's another model. This is a glioma.
7 Again, this compound doesn't normally cross the blood
8 brain barrier, but it does accumulate in brain tumors.

9 So here are some of the images and a fused image
10 along with post-mortem histology slide showing that
11 this compound does appear to selectively accumulate in
12 the normal tissue in vivo.

13 Here's an interesting comparison between
14 the I-124 -- It used to be called NM404. Now it's
15 CLR1404. The company changed the name for some
16 reason. FDG is accumulating at that lesion at the top
17 called I which is an inflammatory lesion. It's not
18 accumulating. The NM404 is not accumulating there.
19 Similarly, there is less uptake in the heart. There
20 is a lot of accumulation of the FDG in the bladder.
21 But there is less accumulation of the FDG in the two
22 tumors in the -- and that's to be compared and
23 contrasted with the image of the 1404 right here.

24 Here's another example. This is an
25 intestinal adenocarcinoma and FDG versus I-124, 1404.

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1 The heart is quite bright in the FDG. The kidneys
2 are illuminated and the bladder has a lot of activity.

3 This is not the case as much with the I-124 labeled
4 1404, plus you see a lot more of the tumor here and
5 that was -- Incidentally, these are the exact same
6 mice in these particular studies. The same mouse is
7 being imaged with one technique and then a different
8 technique. So it's an internal control.

9 There are just some more illustrations of
10 how this agent appears to be accumulating selectively
11 in the tumor area but not in the normal brain.
12 Supposedly it doesn't cross the blood brain barrier
13 and it doesn't accumulate in the normal brain tissues.

14 And that's what these images appear to be confirming.

15 Here's an example of pancreatic cancer
16 imaging, axial, coronal and sagittal. You can see
17 that it does accumulate quite brightly in these
18 particular areas, in that one particular area.

19 Prostate cancer, this is always a
20 challenge for FDG PET, but so far it appears that this
21 1404 compound accumulates in prostate cancer cells as
22 well as the other ones and the interesting thing about
23 this is that it's accumulating in all these different
24 cell lines. I showed you a pancreas adenocarcinoma, a
25 glioma. Here's a prostate cancer. There's something

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1 very interesting about the biology of this particular
2 compound, but it remains to be a fairly elucidative.
3 But hopefully it can be exploited clinically.

4 Here's an example of animal on Day Zero
5 treated with a dose of I-125 label 1404 and you can
6 see the time course, Day Zero, Day Four, Day Nine, Day
7 41 and the comparison was made with the untreated
8 sibling group died at age 21 days after the treatment
9 after the tumor was implanted. So the sibling which
10 was untreated lives 21 days. This animal was
11 euthanized at 80 days and apparently in good health.

12 So to summarize, these phospholipid ethers
13 are selectively taken up and retained by all xenograph
14 and spontaneous tumor models examined to date. And
15 it's quite impressive on that.

16 The tumors, the cancers, take up these
17 compounds with the adenomas, hyperplasias, and
18 inflammatory lesions apparently do not. The uptake is
19 independent of location. So primary tumors take this
20 up. Metastatic tumors take this up. Regional lymph
21 nodes also do.

22 The imaging characteristics of I-124 label
23 phospholipid ether compounds in animal models seem to
24 compare favorably to what we might expect to get with
25 FDG and it enables brain and prostate imaging with

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1 PET, something that we don't presently have routinely
2 available in the clinic and it doesn't accumulate in
3 the inflammatory lesions.

4 There have been a few studies done on
5 humans, I think, about a half dozen patients so far
6 that just demonstrated that you can see where the
7 compound is going in human tumors as just like in the
8 animal models. Formal clinical trials are pending and
9 are expected to start this summer.

10 I just wanted to introduce the staff and
11 the Committee to this new agent and maybe new set of
12 agents that at this very early preclinical phase, at
13 this very early phase, show great promise and
14 potential and I thought would be of great interest.

15 CHAIRMAN MALMUD: Thank you. It was
16 fascinating.

17 Dr. Nag.

18 DR. NAG: What do you foresee are the --
19 implications and radiation safety implications?

20 DR. WELSH: Well, one of the things that
21 we talked about just today was the use of iodine-131
22 in thyroid cancer patients and how if we are going to
23 release them from the hospital we have to be
24 reasonably sure that they're not going to expose
25 people to more than a certain amount per year or

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1 people with metastatic cancer unlike the average
2 patient who gets thyroid cancer ablation. I would
3 imagine that this treatment might be done more than
4 once or twice or three times a year and therefore the
5 exposure to any member of the public might exceed what
6 our limits are per year and therefore I wonder if this
7 is going to have to be an inpatient treatment for many
8 of these people.

9 CHAIRMAN MALMUD: Dr. Eggli.

10 DR. EGGLE: From a clinical medicine point
11 of view, this is really fascinating. I think nothing
12 beats the speed of FDG being able to image a patient
13 90 minutes after injection rather than days. But for
14 the tumors that are poorly FDG avid and prostate was
15 one of your examples certain other cell subtypes like
16 lobular, breast and mucinous colon that are poorly FDG
17 avid it probably has really great progress I would
18 think. It really looks nice. One of the other
19 comments though is the mice were fasted for the FDG
20 studies making the FDG look worse than it would
21 probably look in the clinical situation if the mice
22 had been adequately fasted.

23 But I think this is -- To have other PET
24 isotopes available that allow you to link to molecules
25 that will light up the tumors that FDG doesn't work

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1 for is really fascinating and the potential of this is
2 really fascinating from a clinical point of view, not
3 just for therapy but specifically for diagnosis.

4 CHAIRMAN MALMUD: Dr. Nag.

5 DR. NAG: Have you or any identified any
6 false positives? Have there been updates? You've
7 shown that there were negatives in so many things and
8 positive in a number. But have you seen any updates
9 in any other?

10 DR. WELSH: No.

11 CHAIRMAN MALMUD: So far none. All right.

12 Dr. Schwarz.

13 DR. SCHWARZ: I'm just curious what human
14 tumors you're looking at with the IND trial?

15 DR. WELSH: I had suggested a couple and
16 it was pancreas, glioma, prostate and lung.

17 DR. EGGLI: Again, I would encourage the
18 investigators to look at tumors where FDG works poorly
19 and add breast and colon to that. I mean,
20 bronchoalveolar lung is one of the other cell types
21 that are poorly FDG avid. But from a marketing point
22 of view if you want to break into the marketplace do
23 something FDG can't do which again the bronchoalveolar
24 lung, the lobular breast, the mucinous colon and the
25 prostate which you've shown very nicely. Those are

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1 areas where FDG -- where essentially you don't have to
2 -- where there's no competition.

3 CHAIRMAN MALMUD: But you're speaking of
4 diagnosis.

5 DR. EGGLI: Yes.

6 CHAIRMAN MALMUD: And you're speaking of
7 diagnosis and treatment.

8 DR. WELSH: I think the term they have for
9 it is a theragnostic.

10 CHAIRMAN MALMUD: Yes. Which you could do
11 with a combination of, let's say, I-123 label for
12 diagnosis and then switch to I-131 or I-125 for
13 therapy without having stunned the tumor assuming that
14 it works. And so --

15 DR. SULEIMAN: Yes, I wanted to clarify.
16 This Suleiman. Yes, the FDG is just used for
17 monitoring and basically for possible therapeutic
18 outcome. But this is a therapy and so I would hope
19 that there's some effort at some accurate dosimetry --

20 (Laughter.)

21 -- which we've seen. I mean it's been
22 problematic with the radiotherapeutic pharmaceuticals.

23 DR. NAG: Yes.

24 DR. SULEIMAN: And the other thing just to
25 educate the two clinical endpoints really that the

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1 Agency will probably look for is what progression
2 increase or overall survivability and so I would
3 encourage they focus on trying to keep the studies
4 simple.

5 DR. FISHER: What's the uptake time?

6 DR. WELSH: Don't know the answer to that.

7 In humans, I don't think that the answer is
8 available.

9 DR. EGGLI: From the slides on mice, it
10 was days.

11 DR. FISHER: Was it days?

12 DR. EGGLI: If you looked at the
13 progression of the slides, it was days.

14 CHAIRMAN MALMUD: The ones that had the
15 days labeled on it.

16 DR. FISHER: You need a longer --

17 CHAIRMAN MALMUD: -- number. Well, I-131
18 certainly has it and I-125 also.

19 DR. FISHER: But this mechanism suggests
20 that -- entered like astatine-211 targeting the cell
21 membrane might be ideal.

22 DR. EGGLI: I agree. You can get it
23 targeted quicker.

24 DR. WELSH: I believe that the individuals
25 at the company considered various isotopes and elected

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1 to go ahead with I-131 as their chosen radioisotope
2 because they felt that it had least risk of non-
3 efficacy in early trials and because it's easy for
4 them to manipulate.

5 CHAIRMAN MALMUD: Dr. Eggli.

6 DR. EGGLI: And again let me come back to
7 what I do which is the diagnosis. I think in I-124
8 labeled radiopharmaceutical has huge potential benefit
9 in the diagnostic arena. You know, you may
10 subsequently follow with a therapeutic application
11 with I-131 but there is huge potential in the
12 diagnostic arena with an I-124 label.

13 DR. WELSH: And it would allow dosimetry
14 beforehand as requested.

15 DR. EGGLI: Right.

16 DR. WELSH: And do quantitative
17 pretreatment dosimetry response.

18 CHAIRMAN MALMUD: Any other questions for
19 Dr. Welsh or comments?

20 DR. WELSH: One final point that I do
21 recall being discussed with some of the investigators
22 was in relevance to the difficulty of obtaining
23 isotope. For a group of investigators who have
24 started a company and hope that they'll have a
25 success, there was some serious concern about the

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1 reactor in Ontario going down and the brief limitation
2 that was placed on clinical and research activities
3 and I think they are acutely aware of that and I don't
4 know what the solution is going to be.

5 DR. EGGLI: And the reactor only goes once
6 every five years.

7 CHAIRMAN MALMUD: The I-131 is relatively
8 ubiquitous in terms of its availability for medical
9 use nationally.

10 DR. EGGLI: Until the reactor goes down in
11 Canada.

12 DR. FISHER: With one supplier in Canada
13 Ontario that one reactor goes down and you're out of
14 I-131.

15 CHAIRMAN MALMUD: It hasn't happened yet.

16 DR. EGGLI: Well, the Canadian government
17 shut it down a few months ago.

18 CHAIRMAN MALMUD: Dr. Schwarz.

19 DR. SCHWARZ: I'm curious as to --

20 (Telephone conference announcement.)

21 -- produced the I-124 -- in Wisconsin.

22 DR. WELSH: This is happening --

23 DR. SCHWARZ: The I-124 is being produced
24 in Wisconsin. Who is producing the I-124?

25 DR. WELSH: These studies were done at the

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1 University of Michigan and are they done at Mass as
2 well?

3 DR. SCHWARZ: And in Wisconsin. Correct?

4 DR. EGGLI: Yes, but almost any commercial
5 radiopharmacy these days will cook up I-124 for you.

6 CHAIRMAN MALMUD: I-124, no.

7 DR. SCHWARZ: No, they won't. Just a
8 positron.

9 DR. EGGLI: PETNET will make it for us.

10 DR. SCHWARZ: Well, there are certain ones
11 that will but not everyone certainly. We've made I-
12 124 at Wash U. but we don't routinely ship it. I
13 mean, there are very selective places. So if you're
14 close to one, that's good.

15 CHAIRMAN MALMUD: The interesting thing is
16 that it doesn't really matter at this point because
17 what you want them to do now, what they want to do
18 now, is to identify as a diagnostic agent and --

19 (Telephone conference announcement.)

20 -- as a therapeutic agent -- either I-123
21 for diagnostic or with I-131 and even I-125. So
22 there's a choice of isotopes of iodine other than the
23 positron.

24 When we used to develop
25 radiopharmaceuticals we always hoped we could label

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1 something with iodine because it was so readily
2 available and technetium chemistry is such a dog. So
3 you have to write up isotope and assuming that it
4 remains available to you. You have to be an optimist
5 and assume that it will. It sounds very promising.

6 All right. So, if we may, we'll move onto
7 the next topic.

8 (Whereupon, at 3:55 p.m., the proceedings
9 adjourned to resume in Closed Session.)

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