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NUCLEAR REGULATORY COMMISSION

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ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

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MEETING

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OPEN SESSION

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MONDAY,

APRIL 28, 2008

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

COMMITTEE MEMBERS:

LEON S. MALMUD, M.D., Chairman

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

DOUGLAS F. EGGLI, M.D., Member

DARREL R. FISHER, Ph.D., Member

DEBBIE B. GILLEY, Member

RALPH P. LIETO, Member

STEVE MATTMULLER, Member

SUBIR NAG, M.D., Member

COMMITTEE MEMBERS: (cont.)

SALLY W. SCHWARZ, Member

ORHAN H. SULEIMAN, Ph.D., Member

BRUCE R. THOMADSEN, Ph.D., Member

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

JAMES S. WELSH, M.D., Member

NRC STAFF PRESENT:

STEPHANIE BUSH-GODDARD, RES

CINDY FLANNERY

SANDY GABRIEL, Region I

DONNA-BETH HOWE, Ph.D.

TONY HUFFERT

PENNY LANZISERA, Region I

ROB LEWIS

ANGELA R. McINTOSH, FSME

CHARLIE MILLER

ASHLEY TULL, FSME

MARTY VIRGILIO

DUANE WHITE, FSME

RON ZELAC, Ph.D.

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

FEMILY WILSON, ASTRO

T-A-B-L-E O-F C-O-N-T-E-N-T-S

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

8:14 a.m.

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

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

MS. FLANNERY: Thank you. As a designated federal officer for this meeting I am pleased to welcome you to Rockville for the public meeting of the ACMUI. My name is Cindy Flannery. I am the team leader for the Medical Radiation Safety Team within the Medical Safety and Events Assessment Branch.

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

This is an announced meeting of the committee. It is being held in accordance with the

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

The meeting was announced in the March 18, 2008 edition of the Federal Register. The function of the committee is to advise the staff on issues and questions that arise on the medical use of by-produce material. The committee provides counsel to the staff but does not determine or direct the actual decisions of the staff or the Commission. The NRC solicits the views of the committee and values their opinions.

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

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

making activities.

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

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

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

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

They will be joining us later on today.

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

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

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

Also, I have the great pleasure to formally welcome Mr. Steven Mattmuller, the new Nuclear Pharmacist Representative. Let me take this opportunity to thank all of you for taking on this important role. We really wish you success during this turbulent period in the Materials Regulatory Program. We really are looking forward to the advise you can give us on the regulatory initiatives underway

in security and in safety.

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

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

In the coming year we are going to develop national source tracking system and a web-based licensing system that will really reinvent our regulatory approach and interface with out licensees. The period of increasing expectations on NRC on Agreement States and on licensees regarding material security will continue in the coming year and may easily even amplify.

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

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

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

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

At this point I would like to hand the

meeting over to the Chair, Dr. Malmud.

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

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

MR. LEWIS: I think we can move on.

CHAIRMAN MALMUD: Move on?

MR. LEWIS: Yes, that would be wise.

CHAIRMAN MALMUD: In that case, the next item on the agenda would be a discussion of PET Radiopharmaceutical Production. Sally Schwarz has that item on the agenda.

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

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

operations.

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

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

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

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

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

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

The workhorse of PET is F-18 fluoride.

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

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

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

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

actual cyclotron.

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

MS. SCHWARZ: They are about five and a half to six feet tall. They are not large compared to the older machines that were kind of massive machines. The diameter is about, I want to say, eight feet in diameter. Again, this is an example when they were installing our machine.

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

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

CHAIRMAN MALMUD: Sally.

MS. SCHWARZ: Yes.

CHAIRMAN MALMUD: May I take this moment to interrupt you. I'm sorry. We have an important issue to address and Dr. Miller is here to address it. Just remain where you are for the moment and I'll introduce Dr. Miller. Charlie Miller.

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

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

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

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

For example, Part 35 T&E. She shaped the alternate pathway for authorized nuclear pharmacists. New Modality Subcommittee she served on and the Dose Evaluation Subcommittee. Without further ado, what I would like to do is present you with this certificate to thank you for all your wonderful service to the committee. We are sorry to lose you.

MS. SCHWARZ: Thank you very much. I have enjoyed the time that I have served on this committee. It has been a true learning experience. I mean, it has opened my eyes to a number of issues, overall regulatory direction, and I really feel that certainly you have broadened my horizons.

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

CHAIRMAN MALMUD: Thank you, Dr. Miller. Thank you, Sally. Sally, the entire committee seconds

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

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

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

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

This is, again, the ion source. What we do is we use hydrogen gas and there is an electrical field. The gas is ionized and essentially then there is a split opening in this source. Actually it is placed when the machine is paused in the center here. Again, these ions are pulled into the machine due to the current.

This is just an example of we have produced the F-18 fluoride. Then we have to move it from the cyclotron, from the vault where it's located. Again, just as an aside, the actual exposure of the machine, these newer machines for running duel targets, 60 MeV beam currents. If we open the door

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

Then, again, if the machine is turned off it is essentially not radioactive as you turn it off. I mean, it might be one to five MR per hour but, again, relatively easy to work in this area. Then the isotope has actually brought shielded conduits under the floor up to the synthesis modules. Again, these are lead shielded modules -- excuse me, hot cells where we contain our modular system

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

The product port is connected to a sterile pyrogen-free vial that is located in the lead shield. This is then what we do only having to open this ante-room door rather than the actual hot cell to access the final product again reducing exposure to the personnel who are working in the area.

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

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

MS. SCHWARZ: We don't do that.

DR. VETTER: Just say very high.

MS. SCHWARZ: It is very high. I mean, we are working -- it depends, of course, on our starting material of our synthesis nodule. We start production for FDG in our facility, and we are not distributing, with 4 curie F-18 fluoride so if it would be in the middle of that synthesis, it would be extremely high. Actually, one of our SOPs is that under no circumstances are we to open those hot cell doors.

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

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

This is just an example of the FDG module. This one happens to be made originally by coincidence of Belgium metal which now has been taken over by GE. It's a wonderful module. As you can see, it's kind of color-coded reagents which are batch produced like a pharmaceutical batch of product for each of the reagents used in this synthesis.

We have a chemist that comes in when we begin our cyclotron operation at 4:00 in the morning. We run until about 6:00. We have a chemist that comes in to set up these modules at 5:30, 5:15. Again, what they are doing is putting all of the lines in place, the reagents in place. Then once we are ready, we close the hot cell door and the fluoride is then brought from the cyclotron under pressure, delivered directly to the box so there is no handling of the radioactive materials.

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

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

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

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

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

it is significant quality control.

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

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

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

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

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

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

If there is a problem with the final product testing, we then have to go back and revalidate our process if we find it's not a sterile product. I will tell you that in all the years I've been doing this we have not had non-sterile products. We have had operator errors. We have had to reinoculate our products to retest the final product. Our actual products have been sterile so processes are well-defined in terms of what we are preparing for humans.

Also the bacterial endotoxin test is

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

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

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

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

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

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

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

Again, this image on your left is a normal

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

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

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

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

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

We do use the DOT transport labels even though we are traveling within out university license. We are not going exterior. Later in the day our radiation safety truck actually picks up the bulk of our product and delivers it by regular DOT transport.

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

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

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

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

You can use either naturally occurring nitrogen irradiation with deuterons to make the O-15 or enriched nitrogen irradiation with protons to make O-15. This, of course, when you are dealing with enriched target materials to produce an isotope it's always more expensive so we prefer if possible to do this N14 irradiation.

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

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

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

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

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

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

it's over palladium catalysts. We do produce water on site.

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

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

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

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

Again, we are going to use these pharmaceuticals to identify a risk factor for stroke. We are going to look for the amount of increased oxygen extraction fraction in the brain. Again, this is a noninvasive technique and something that cannot be performed without the use of these radioactive materials.

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

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

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

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

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

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

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

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

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

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

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

this particular production is to use carbon dioxide. That is what is made in the cyclotron. We then mix it with methylmagnesium bromide to make this intermediate.

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

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

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

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

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

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

limited dose to our personnel.

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

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

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

This is just a comparison. As I

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

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

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

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

Does anyone have any questions for me?

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

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

MS. SCHWARZ: That's correct.

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

I'm sure there are some questions for you. Dr. Vetter.

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

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

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

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

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

MS. SCHWARZ: Yes, yes, yes.

CHAIRMAN MALMUD: Dr. Nag.

DR. NAG: These are very short-lived

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

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

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

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

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

DR. NAG: Yes.

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

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

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

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

MS. SCHWARZ: Exactly. They do that. They really do have contracts with air carriers. Each of these companies distribute their materials through transport.

CHAIRMAN MALMUD: Dr. Welsh.

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

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

DR. WELSH: I think I meant Medicare reimbursement.

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

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

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

MS. SCHWARZ: Oxygen-15?

CHAIRMAN MALMUD: Yes.

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

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

CHAIRMAN MALMUD: Thank you.

Yes, another question.

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

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

CHAIRMAN MALMUD: Yes, Dr. Fisher.

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

MS. SCHWARZ: How effective is it?

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

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

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

DR. FISHER: It's a linear accelerator.

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

DR. FISHER: It's evolving technology.

MS. SCHWARZ: Right.

CHAIRMAN MALMUD: Any other questions?

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

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

What he is doing is looking at how the

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

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

MS. SCHWARZ: You're welcome.

CHAIRMAN MALMUD: Congratulations again.

MS. SCHWARZ: Thank you very much.

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

MS. TULL: Good morning.

CHAIRMAN MALMUD: Good morning.

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

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

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

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

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

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

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

For No. 2, NRC staff should revise the regulations so that board certified individuals, who were certified prior to the effective date of recognition or were certified by previously recognized boards listed in Subpart J of the previous editions of Part 35, are grandfathered.

This is in regard to the AAPM of the Ritenour petition. This is pending and is predecisional as well so I think everyone knows where that one is.

For No. 4, NRC staff should reduce the 200-hour radiation safety training requirement to 120 hours for individuals seeking authorization under the alternate pathway in 10 UFR 35.390. This was not accepted. We received a management decision on this. Something that was decided in 2005 between the Agreement States, ACMUI, NRC staff. 200 was a compromise so it is going to remain at 200. Any comments? Okay.

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

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

DR. NAG: Can you clarify all equivalent is for what kind of things?

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

Ralph.

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

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

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

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

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

MS. FLANNERY: That's right.

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

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

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

and will be put in a User Need Memo for consideration for future rulemaking.

The next rulemaking should start later this year as the current rulemaking that is on 3540 and 3045 which is directives and medical event reporting. We are currently working on that. As that begins to come to a close we'll start a new rulemaking. These items would be considered in that rulemaking to give you a better idea.

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

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

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

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

CHAIRMAN MALMUD: Mr. Lieto.

MR. LIETO: When was this decision made?

MS. TULL: The interpretation from Office of General Counsel was made two months ago.

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

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

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

MS. TULL: Yes.

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

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

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

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

DR. NAG: I think now.

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

CHAIRMAN MALMUD: Would a member of the committee, other than the Chair, wish to make that motion?

DR. THOMADSEN: So moved.

MR. LIETO: Second.

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

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

DR. THOMADSEN: That's the motion.

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

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

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

going to reject this if you make the current motion that is on the table."

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

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

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

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

MR. LEWIS: I think you need to see the

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

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

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

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

CHAIRMAN MALMUD: Thank you. Our motion

has been moved, seconded, and discussed. Any further discussion of the motion?

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

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

PARTICIPANT: Ten.

MS. TULL: Is it updated?

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

MS. TULL: Okay.

CHAIRMAN MALMUD: That was the January 10th memo.

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

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

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

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

ALL: Aye.

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

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

CHAIRMAN MALMUD: Please move forward.

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

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

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

doesn't have to be with the particular type of microsphere. NRC did not accept that piece so if you want to use TheraSphere you need to go get TheraSphere training from MDS.

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

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

No. 12, NRC staff should delete the attestation requirement for Y-90 microsphere users and incorporate a requirement in the second paragraph of the guidance for individuals seeking authorization to provide and retain documentation of the completion of training. This was Dr. Williamson's recommendation before he left and this was accepted and has been incorporated into the proposed guidance that you will

see tomorrow.

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

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

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

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

No. 17, NRC staff committed to consult legal counsel to determine the feasibility of discussing PRM 35-20 (Ritenour/AAPM petition) with

ACMUI members in a closed executive session. This was discussed at the last meeting and it's also on the agenda for this meeting for a status update on that.

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

No. 19, NRC staff should engage ACMUI in a discussion regarding the review of operational events and data and work towards a goal of minimizing therapeutic medical events, if directed by the Commission to do so. The Commission did not direct this. It was pulled out of the staff requirements memorandum so we are not taking any action on this item.

Yes, Dr. Malmud.

CHAIRMAN MALMUD: I just wanted to make a comment actually that all the committee members know that I did meet with the Commissioner regarding the issue of fingerprinting. The response from the Commissioner was that this recommendation came from a different authority, a higher authority. Therefore, it was not in the NRC's purview to challenge it.

MS. TULL: For 19 or for 18?

CHAIRMAN MALMUD: The fingerprinting issue.

MS. TULL: So for 18. Okay.

CHAIRMAN MALMUD: Yes, fingerprinting.

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

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

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

CHAIRMAN MALMUD: No. 20.

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

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

No. 22, ACMUI supports grandfathering for individuals who had previously been determined to be

trustworthy and reliable and granted unescorted access. This was not accepted and orders were mailed back in October.

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

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

For No. 26, NRC staff should maintain Compatibility B for training and experience requirements to ensure that authorized individuals may cross state borders and practice throughout the U.S. This is accepted. This is NRC's current practice and

will remain that way.

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

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

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

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

No. 31, NRC staff should require

experienced RSOs and AMPs to receive additional training if the individual is seeking authorization or responsibility for new uses. This is accepted and will be put in a User Need Memo for consideration for rulemaking. Any questions?

No. 32, NRC staff should not require experienced RSOs to obtain written attestation to become authorized or have responsibility for new uses. This is also accepted and will be in a User Need Memo and will be considered for a rulemaking.

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

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

MS. TULL: Dr. Vetter.

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

If you go back to the guidelines from NCRP

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

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

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

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

DR. VETTER: They would have to be hospitalized.

MS. TULL: They can't be released.

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

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

Also there are some new treatments that are coming out where there are multiple therapeutic treatments given over the course of the year and might either preclude all those be given or that they all would have to be set up such that the patient is hospitalized for each of those treatments. There was, I think, some valid concerns about not increasing this

or leaving the time specification off.

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

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

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

The international foundation for this regulation was clear. The intent in our statement of

considerations was clear and the people that actually wrote the rule their intent was clear. We view this not as a change in policy but as a clarification that this has always been the policy.

CHAIRMAN MALMUD: Dr. Nag.

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

MR. LEWIS: That's fair enough.

MS. TULL: Sure.

CHAIRMAN MALMUD: Would you like to make a motion?

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

CHAIRMAN MALMUD: You want to insert the word promptly in there?

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

CHAIRMAN MALMUD: Is there a second to the motion?

DR. WELSH: Second.

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

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

CHAIRMAN MALMUD: Thank you.

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

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

For No. 35, NRC staff should not revise 10

CFR 35.491 which was intended for ophthalmologists to include training and experience for the new intraocular device. Instead, NRC staff should regulate the new intraocular device under 10 CFR 35.490. Same thing on this. We are still going to be working on some words when rulemaking comes around.

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

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

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

No. 39, NRC staff should revise the

microsphere guidance to include a paragraph referencing medical event reporting for microsphere use. (10 CFR 35.3045). This is accepted and is in the proposed guidance for discussion tomorrow.

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

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

No. 42, NRC staff should revise the microsphere guidance to add a paragraph which states, "training in manufacturer's procedures, commensurate with the individual's duties to be performed, must be provided to individual preparing, measuring, performing dosimetry calculations, or implanting

microspheres." This is accepted and is in the proposed guidance that will be presented tomorrow.

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

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

No. 44, ACMUI recommended for each training program, including radiology, radiation oncology, radiation physics, and nuclear pharmacy, that the curricular requirements be established by those boards, which recognize the importance of the NRC standards for radiation safety and radiation physics. This was not accepted and the comment here was that NRC sets general topics and a minimum number

of hours. We are really only focusing on the radiation safety and not all curricular topics. Any comments or questions?

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

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

Dr. Vetter.

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

CHAIRMAN MALMUD: You are correct.

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

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

The reason the challenge is to the excessive number of hours is that the boards currently in their training programs are teaching residents, particularly in the field of radiology technologies that did not exist only a few years ago and, therefore, there is a time limit as to how much time can be given to each subject.

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

DR. VETTER: Yes.

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

Yet, the opinion of educators whose lives are devoted to these topics are rejected. It is a challenge to our understanding. That is the feeling of the committee.

Cindy, did you raise your hand?

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

DR. ZELAC: Ron Zelac. I'm a little bit puzzled by the position to the extent that there is

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

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

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

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

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

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

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

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

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

Mr. Lieto.

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

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

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

It has now become actually the training

and experience requirements for the boards and for the residents to get board certification. I think the number of hours that have gone into this have become very, very prescriptive and I think this is where the renewed objections are arising from.

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

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

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

MR. LIETO: I didn't mean to steal your thunder from earlier but I think the emphasis is how the NRC is recognizing the boards. This relates to

the board recognition aspect, if I'm not mistaken about this agenda item, this recommendation item No. 44. It is not meant as an alternate pathway.

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

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

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

So consistently we have tried to emphasize that for us the boards having a workable pathway to

get board certified as soon as possible after training is the best way to determine that the physician or the physicist or whomever has knowledge. Sitting in a classroom 200 hours doesn't demonstrate knowledge. That's where we get hung up on the number of hours.

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

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

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

them again becomes an issue of having established a number of hours required training under the ultimate pathway for one in five individuals.

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

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

No. 46, ACMUI should form a subcommittee to further discuss the proposed change to 10 CFR 35.75 to release patients, if the total effective dose equivalent to any other individual from exposure to the released individual is not likely to exceed 5 mSv/year. The subcommittee includes: Dr. Vetter, Dr. Eggli, and Dr. Fisher. The subcommittee reported back to us last October, the next day, the second day of

the meeting that they reported back to us.

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

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

Sally.

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

DR. NAG: Money.

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

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

MS. SCHWARZ: What alternative does the patient have?

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

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

DR. NAG: Yes, I would assume that your

hospital then does not permit low dose rate brachytherapy. Low dose rate brachytherapy in the hospital is usually three days.

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

DR. NAG: But it should be similar then.

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

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

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

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

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

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

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

No. 49, ACMUI should forma subcommittee to annually review byproduct material events, perform analysis, and report to the full Committee. NMED data should continue to be presented to ACMUI at the fall meetings, and the subcommittee should analyze the data presented at the fall meeting in order to provide a full report at the spring meeting.

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

No. 50, ACMUI byproduct material events

subcommittee should publish reports as necessary to ensure end-users receive the message. That is at the discretion of the subcommittee so I will leave that open and ongoing for you to decide.

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

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

Any questions or comments on any of the items?

CHAIRMAN MALMUD: The committee thanks Ashley Tull for an yeoman's job on presenting these 51 items.

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

CHAIRMAN MALMUD: We look forward to it.

MS. TULL: All right. I'm handing out the

presentation that Rob Lewis is going to give. These are the slides right now because he's about to start.

DR. NAG: Mr. Chairman.

CHAIRMAN MALMUD: Yes.

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

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

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

DR. NAG: If need be I am prepared to issue what the problems are.

CHAIRMAN MALMUD: Thank you. Can we squeeze that into the agenda, Cindy?

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

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

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

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

MS. FLANNERY: I guess I just want to make sure I understand this right. Are you shortening your

time or are you getting --

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

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

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

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

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

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

CHAIRMAN MALMUD: Thank you. We will look

forward to hearing that within the time allowed for your presentation.

It is now 10:13 and Ashley's presentation has allowed us to move to the next item on the agenda. You have some slides to present?

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

CHAIRMAN MALMUD: You want to do the break first?

MS. FLANNERY: That was on the agenda.

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

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

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

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

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

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

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

Before I go any farther, I would like to thank the efforts of Dr. Vetter and Dr. Nag

especially, who looked at the issue on behalf of the Committee operating as a sub-group and gave us very quick comments that really helped us communicate the messages that are in the NAS report, especially the impacts of those recommendations upon the practice of medicine.

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

The next recommendation is -- the finding is that the NRC ranks hazards in source security based upon deterministic health effects, prompt fatalities related to the misuse of the radioactive sources, and the Committee felt that NRC should also consider the potential of the sources if they were misused to cause economic and social disruption. This is the only

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

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

There are about 1100 blood or research

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

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

What the NAS committee did not do, though, is they gave the what, you know, the lighthouse. They didn't tell how or who or how -- you know, the implications. They left that up to the government as

a whole to determine what's the best path forward. They did suggest three specific actions. First of all, to discontinue licensing new cesium chloride irradiator sources and their point there is don't exacerbate an existing problem by letting out more sources regardless of how low the numbers may be, because technology do exist that could be an alternative.

The second is put in place incentives for decommissioning the sources. Like I said, the sources have been out and in use for many years. Often there's no incentive for the hospital or research facility to buy a new piece of equipment, whether it be x-ray or cobalt or another form of cesium. There's no economic incentive to get rid to the source, it's working fine for their purposes. And prohibit the export of cesium chloride sources to other countries. This measure is, for example, if the U.S. were to take action to increase the security domestically for cesium chloride sources -- specific to cesium chloride sources, we don't want to create a situation where people start buying an alternative and send the cesium chloride sources to a developing country and our overall world or domestic security overall might actually decrease.

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

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

sources and bring those alternatives back to the state of the art with regard to calibrating which wells to bring in, because it's a big investment decision of where to dig, for example.

The NRC has, as I mentioned, we have taken the recommendations. They are what they are. We're going to move forward with the recommendations and our primary vehicle to move the issues forward is the established NRC and Interagency Policy Act task force. As I mentioned, there's 14 different federal agencies represented on the task force. It's not just regulatory. It's the broad suite of all federal activity and there are two state organization because of course, these issues bear upon agreement states as well. And the task force has specific subgroups that are active; a subgroup on radiation sources that will consider the social economic aspect that the NAS Recommendation 2 mentioned. There's a subgroup on cesium chloride specifically. They have a product due in the fall.

There's a subgroup on public education, which is somewhat unrelated to the NAS finding and finally, there's a subgroup specific to alternative technologies maybe even beyond cesium but all alternative technology sources. It also has a product

due about a year from now. All of those efforts, as I said the NAS told us what, what their opinion is of what should be national policy and the Energy Policy Act is the best vehicle we have to both get a U.S. Government-wide opinion of what the national policy should be and also the how. Who should do things and which things are within the rules and responsibilities of the various agencies and who should do them when, what time frame should they all be done.

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

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

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

impacts of new regulations or regulations to phase things out. And the task force is going to be seeking help from the industry on determining those impacts and the magnitude of them.

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

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

MR. HUFFERT: Not at this time.

CHAIRMAN MALMUD: Thank you. Dr. Vetter?

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

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

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

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

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

And frankly, you know, many doctors we've talked to are in two camps; those that swear by x-ray and those that swear by cesium chloride blood rating. And so we hear it from both sides. I don't know that Congress has heard from both sides and certainly any -

- we are outreach. We're trying to reach out to the industry, both the medical industry and the source industry to make sure that they're properly energized. The government, you know, will have to take these recommendations and propose a path forward to get it in front of people and get feedback on the impacts.

CHAIRMAN MALMUD: Dr. Nag.

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

One is that the one thing is cesium chloride. However, the public is likely to hear the word cesium. Now, cesium, you can have cesium-131 and cesium-137 and you can have the cesium-137 low life in the blood which is quite different from the cesium-137 used for low dose rate radiotherapy with more encapsulated. And my fear or the fear of the subcommittee and hopefully the entire ACMUI, is that the public will only hear cesium and therefore, will view cesium-137 encapsulated and cesium-131 which is used for prostate implant as a new source in the same light, and therefore, would try to eliminate those and

will definitely not what the NAS wanted and not what the ACMUI wants.

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

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

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

MR. LIETO: That was going to be one of my --

CHAIRMAN MALMUD: Mr. Lieto.

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

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

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

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

DR. NAG: And the other comment, I think, that the subcommittee had was that the NAS has

mentioned the use of alternative sources, the use of electrically or simulator-based sources, but has not really dealt with adequately the impact of that, the cost of that and also the effectiveness of that. Some of these things can be a replacement, an alternative, but may not be as effective and you know, that has not been -- that is a strong recommendation that we would like to make. Any other --

CHAIRMAN MALMUD: Dr. Fisher?

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

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

one goal of this report.

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

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

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

MR. LEWIS: Well, I think that they would not be, insofar as they were greater than Class C low level waste, there would currently be no permanent disposal option but the Academy would probably view

getting them in the hands of the government, whether it be through DOE or somehow getting them out of the hospitals and into a more secure place for temporary storage pending disposal is some of the incentives to push full incentives and I think we have to explore that.

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

MS. GILLEY: Thank you.

CHAIRMAN MALMUD: Dr. Thomadsen.

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

MR. LEWIS: If it was a government-wide solution, I think that the amount of material we're

talking about here is very small. It's big for us but it's small in compared to the amount of sources that DOE may already stored at some of their labs. You know, Hanford or Savannah River have very large inventory sources of plant fuel already, high level waste. So I think that that's a good point that needs to be considered when it's consolidated but I think as I said, it's a government-wide solution and looking at the totality of the issue that these will be dwarfed in the tidal wave of other sources that exist.

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

CHAIRMAN MALMUD: Dr. Welsh.

DR. WELSH: I have a question about the statement that alternatives exist for cesium-137 at this point and these questions might reflect my ignorance on the subject as a whole but I understand that cesium-137 has been the standard in medical practice for blood irradiators. It has a 662 keV gamma. It's got a long half life but we can be comfortable with our clinical experience with the

energy and the dose rate.

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

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

Costs, in administrative costs, I'm pretty sure x-rays is rather higher, I've hear double. But in terms of the technologically effectiveness, technical effectiveness, I think the studies have shown that either one can be used. I think that that's for blood irradiation. I think that the same end use may be a little more tricky for research.

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

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

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

Now, on the alternative technology sub-group of the task force, we asked this question to representatives of the NIH and one of the people said, no, that they're quite happy with cesium and they aren't willing right now to make that switch. So we

have antidotal evidence, but I think the position of the National Academies was that they are effective.

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

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

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

CHAIRMAN MALMUD: Dr. Vetter is one. Who else on the committee is involved with the use of cesium regularly in both research and in blood

irradiation. We have two more, Dr. Fisher and Dr. Thomadsen. I'm sorry, and Ralph.

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

CHAIRMAN MALMUD: You do.

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

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

MR. HUFFERT: It's excellent.

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

MR. LEWIS: Thank you. That's all the

comments I had, unless there's any more questions for me.

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

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

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

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

MR. LIETO: I just had a quick question. Is the full report available, because we've got summaries and links to summaries and those types of things but I don't think the links that we have are to the actual report or is that sort of still classified?

MS. TULL: This is Ashley. I sent you

guys a copy. It's a link to the NAS site. It's the full report and I actually have a binder with three copies if you guys want to look at these or take these over here. You have to kind of log in with your e-mail address to get that link to work.

MR. LIETO: Okay.

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

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

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

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

And therefore, the new Perfexion gamma knife had to be placed under 35.1000 as a new modality. At the last ACMUI meeting, it was recommended that the 35.600 be modified such that it will be -- enable the Perfexion to fulfill the

requirements. The subcommittee will -- Dr. Thomadsen, Dr. Welsh, Dr. Lieto and Dr. Gilley and we had requested three other people who have experience with the Perfexion to aid as consultants and they were Dr. Arapino, Dr. Getz and Dr. Shoe (phonetic).

Especially Dr. Eno, who is at the University of Pittsburgh and has used this a lot, has helped us very much in providing many of the wordings. So basically, if you will see the handout under Section 5, we have made just some minor modifications whereby we have used wordings that are -- instead of having the word helmet there, we have a more generalized wording such that not only the new gamma knife, the Perfexion model, but also the Chinese gamma knife that is coming out or that is out will also be able to fulfill it, so we have made all the wording very generic instead of being specific to the Elekta gamma knife.

I will not go through each and every word but basically on page 1, what we did is that we made it applicable to all models, so you can see how we deleted just the word. And for example, on page 2, we just put the word polymason (phonetic) output and polymason system rather than putting trunnions and helmets. So this way it would be more generic and all

encompassing, and throughout the entire document, we just changed the words so that it would be all encompassing. So if you have any questions on any of them, basically it's just changing the wording of helmet and trunnions and replacing them with more generic words and that was all that was needed and we felt that having it more generic would allow at least most of -- all the current forms of gamma knives now and hopefully many of the future gamma knives to be able to accommodate this 35.600.

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

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

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

CHAIRMAN MALMUD: Dr. Welsh.

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

DR. NAG: I don't know. I mean, that was something that one of the physicists consultants

brought up that the Chinese version and I think Bruce might know.

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

CHAIRMAN MALMUD: Other questions? Thank you.

DR. NAG: As I had mentioned, I thought that this would take a very short time and that's why I would have a few minutes. What I would like to ask the ACMUI is that there was a -- there was a 535 last language for permanent brachytherapy that was sent to all of your on and not for public knowledge on February 21st, 2008. That document went through some of the wordings that would be subject to rulemaking for permanent brachytherapy and this would be under 10 CFR 35.40 and 35.3045. If you don't have the detail with you now, I won't go into detail, but what I would like is to request that the ACMUI have a separate teleconference to discuss this because I feel that some of the wording may be problematic and I would like to have the full ACMUI members discuss that and if possible, to have in that discussion one or two more consultants who do brachytherapy to give a more representative view. So that is a motion that I would

like to make.

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

DR. WELSH: I second.

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

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

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

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

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

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

DR. VETTER: And what's the time line on the ruling?

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

CHAIRMAN MALMUD: Mr. Lieto?

MR. LIETO: Yeah, I know what Dr. Nag is referring to but I'm just wondering, it might be a little bit premature here. Maybe, because I know that people commented on it, I know I did and others and I

think it was sent out to Cindy. I think maybe what we ought to do is see how they incorporate all the comments, sort of as an advanced publication to rulemaking or something like that to see how they're taking the comments and suggestions.

DR. NAG: That came out last week.

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

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

MR. LIETO: All right.

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

CHAIRMAN MALMUD: Cindy?

MS. FLANNERY: A couple of things. You were asking about having members of the public participate in a closed session.

DR. NAG: Consultants.

MS. FLANNERY: Consultants.

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

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

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

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

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

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

DR. NAG: Whatever would work.

MS. TULL: That's what I was trying to explain a second ago. If you do a subcommittee meeting, there is no issue on it being closed to the public and you can consult with others. I don't know about actually having them on the call but as far as

sending them an e-mail and asking for their comments, incorporating that into your subcommittee discussion, we can close off a subcommittee meeting. I can set up a teleconference.

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

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

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

DR. NAG: The purpose would be to bring my concern as well as the concern of others who do a lot of permanent brachytherapy because if you're not doing a lot of permanent brachytherapy, you may or may not know all the implications of the wording of people who attend. So, I mean you have someone who's never done permanent brachytherapy to be in that committee would

not really add much, but someone who's done a lot and sees some of the indications would really be meaningful. So I want to have some meaningful input and not just mine.

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

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

If it is a public meeting, whether it -- I should say if it is a full committee meeting, whether it's public or whether it's closed, it has to be announced. And we're talking about a month out. And if the purpose is to, you know, bring the concerns and recommendations to NRC, that really should be a full committee. And you can meet as a subcommittee before then to get everything together to prepare for that full committee meeting, but a full committee meeting, whether it's closed or open, has to be announced, but we can certainly arrange that if that's what you want

to do.

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

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

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

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

DR. NAG: Right.

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

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

CHAIRMAN MALMUD: You would prefer a closed committee.

DR. NAG: Closed subcommittee meeting and then if we need to have a -- by that time, it may be

that we would be able to put it on the agenda for the next full ACMUI meeting in October.

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

MR. LEWIS: Let me suggest a third confusing alternative. In the past, when we have a difficult rulemaking issue, we have issued as part of a meeting announcement, a discussion draft which describes an issue that people can come to the meeting fully aware of the options and the issue without actually getting into, you know, marking up draft rule text. And in those circumstance, the issue can be fully described as part of the meeting materials in a public way and that may be a path that the committee

could pursue. It's your discretion but I just wanted to make sure that was on the table.

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

DR. NAG: Not fully.

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

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

I would -- yeah.

DR. NAG: The draft that was sent out in February of 21, was a public document and we can have our discussion based on that public document of February 21st, which everyone has and the public has. And for the concerns that we have, that is all that is required to address some of the concerns.

CHAIRMAN MALMUD: So that, therefore, if I

understood you correctly, you are proposing to have a subcommittee meeting referencing the document which was a public document and not the detailed background material which was not public.

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

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

DR. NAG: Right.

CHAIRMAN MALMUD: And that's your motion.

DR. NAG: Right.

CHAIRMAN MALMUD: Is there a second to that motion?

DR. THOMADSEN: I'll second it.

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

MR. LIETO: Yes. In order for him to voice the concerns with the proposed rule, I mean, it was my understanding it was the implementation in the proposed rule that's raised the concerns.

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

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

MS. FLANNERY: That's correct.

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

MS. FLANNERY: Correct me if I'm wrong, but you were just sent a pre-decisional document recently, within the last couple weeks, I believe, and that would have incorporated your comments to the preliminary open document, preliminary draft language;

is that correct, Ron?

DR. NAG: Which is not public.

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

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

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

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

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

CHAIRMAN MALMUD: Dr. Vetter?

MR. LIETO: I don't see the need for a subcommittee meeting at this time because I think what we need to do is get Dr. Nag's specific concerns with this document that was just released as pre-decisional to the committee, all right, and maybe go from there.

Maybe the concerns don't require a committee meeting. I mean --

CHAIRMAN MALMUD: Dr. Vetter?

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

MS. TULL: Yes.

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

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

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

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

CHAIRMAN MALMUD: Sally.

MS. SCHWARZ: I have a question in regard to the possibility of just discussing this at the committee. Will there be a portion of the meeting that will be closed that this document could be discussed within the next two days and then from that point, you can make your --

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

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

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

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

DR. NAG: I think it would be best if we have a separate subcommittee meeting, a small subcommittee. Those of you who want to be on the

subcommittee, in addition to the radiation oncologists, are welcome to be on there. And, you know, that will have the full implication because when you get some of the comments back and so forth, you don't have a full discussion on some of the implications. Some people can comment back and so forth but not the full discussion.

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

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

DR. ZELAC: Just a few things that might help in resolution of this issue. First is, that the proposed rule which you have seen a pre-decisional copy of, is working through the concurrence chain now and the intent is to, of course, have that published as soon as possible which is likely to be in very early June.

So at that point, the document becomes

public and it's available for comment from everyone who would have opportunity to see it and interest in it, including the advisory committee, individual members of the advisory committee, whatever. Any input with respect to what it is at this point is probably not going to have any impact on the proposed rule itself. In fact, I could almost say with assurety from my level that the proposed rule is going to go out as it is now for comment.

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

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

DR. NAG: In that case, what we could do is have a full committee meeting before the fall meeting but after the publication of this public draft, so that we can discuss some of the implications. None of this are going to be changed between now and the publication of that draft.

CHAIRMAN MALMUD: So your recommendation

at this point is that we await the publication of the document for the public at which point comments are invited from all parties, including this committee itself and make -- and have a conference call at that point regarding the issues.

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

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

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

CHAIRMAN MALMUD: And that's your preference above waiting for it to be public and then

having a subcommittee or a committee, either one, via telephone to respond to it.

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

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

MR. LIETO: No, just rubbing my temples.

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

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

Second thing is that the proposed rule, which will be going out reflects as best as we and staff have been able to do, the input, the specific recommendations of the Advisory Committee, which were, of course, based on the input and recommendations of a subcommittee. So we have tried on staff level to look at the advice from the Advisory Committee and incorporate that into appropriate rule language which you have had an opportunity to see in terms of what

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

CHAIRMAN MALMUD: Dr. Nag?

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

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

DR. NAG: If everything goes on time and we are aware on the first day and then we immediately ask for the sub -- a committee meeting, maybe it's possible but I am somewhat -- you know, like many of these things, the ACMUI members are not aware that

this one was circulated. You know, we get so many e-mails that some of these things we may not even know, you know, are out.

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

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

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

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

DR. NAG: If possible --

CHAIRMAN MALMUD: If possible.

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

CHAIRMAN MALMUD: Addressing only the issues that were made public and not -- obviously, not addressing the issues that are not yet public. That's Dr. Nag's recommendation. The concern is that this

may be -- the other opinions we're hearing are in opposition to this because the concern is that a complete discussion will not be able to occur because the details are not yet public and therefore, cannot be brought into the discussion, and that there will be an opportunity which is a 75-day period following the publication of the draft document.

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

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

CHAIRMAN MALMUD: Two weeks.

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

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

MS. TULL: Thirty.

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

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

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

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

MS. TULL: Full, yeah.

DR. THOMADSEN: I just wanted information on that.

CHAIRMAN MALMUD: Any further -- Dr. Vetter?

DR. VETTER: I do have a little bit of a concern about not having this noticed in such a way that stakeholders as a whole could see what's going on here and have an opportunity for input. Secondarily, if it's a subcommittee, I think the charge has to be extremely specific and I haven't heard a charge yet.

So I think we're getting the cart before the horse scheduling a subcommittee meeting when we don't know exactly -- I don't, I'm still confused about exactly what the charge would be and who would be on the subcommittee. So those two things bother me a little bit about the motion.

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

DR. NAG: To answer your question, I think the charge would be to discuss the Part 535 on permanent brachytherapy, the proposed ruling on the permanent brachytherapy and that was already made public on February 21st and the subcommittee member would be any member of the ACMUI but at the very least, the ones who are involved in permanent brachytherapy and that would be myself, Jim Welsh and Bruce Thomadsen and anyone else who have knowledge of permanent brachytherapy should be included.

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

CHAIRMAN MALMUD: Care to call the question? All if favor of the motion? Three. Opposed? Four. Abstentions.

MS. GILLEY: I can't vote yet.

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

DR. NAG: That's fine.

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

DR. VETTER: Dr. Howe has a comment.

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

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

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

DR. HOWE: Yes.

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

DR. NAG: Sure, that's fine with me. Can I request Ashley or whoever in the NRC staff to specifically remind when the request comes. Sometimes you know, we don't always, you know, see it in bold,

to let us know that this was -- this is coming out on this and this date.

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

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

MS. TULL: Sure.

CHAIRMAN MALMUD: Thank you.

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

CHAIRMAN MALMUD: She'll send you an e-mail and then you can contact her regarding what you see is necessary at that point. Do you have another comment, Dr. Zelac?

DR. ZELAC: Just a suggestion, since you're all assembled now, it might be prudent and

worthwhile from a time point of view, to try to set up a meeting now.

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

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

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

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

CHAIRMAN MALMUD: All right.

DR. NAG: That's fine with me.

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

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

CHAIRMAN MALMUD: Yeah, all right.

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

CHAIRMAN MALMUD: All right, Dr. Nag's request is for a full committee meeting. Is there a second to the motion for a full committee meeting? This will be teleconference. It's seconded. All in

favor? Any opposed? The motion carries. Thank you, Dr. Nag. Thank you, Dr. Zelac, for the recommendation and --

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

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

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

CHAIRMAN MALMUD: Now, Dr. Howe?

DR. HOWE: The subcommittee has presented its draft of the proposed changes to the gamma knife. It's important for the NRC staff to know what the committee wants to do with this. So if you could give us an idea of whether you want to have us include this in a user need memo or any other action.

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

DR. THOMADSEN: I think the intent of the subcommittee was to address the concern of the staff that we present to them suggestions for how to make

the rules generic enough to fit all of these types of units. So I would assume that the -- since this committee set up the subcommittee to do that, that the intent of this committee is that the recommendations be propagated into rule.

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

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

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

6. BYPRODUCT MATERIAL EVENTS SUBCOMMITTEE REPORT

MEMBER LIETO: Since we are loaded up here, I guess we can get started. My name is Ralph Lieto. I am Chair of the Medical Radioactive Material Events Subcommittee. We provided data preliminarily at the October meeting, and this was our Subcommittee report.

Subcommittee members are Debbie Gilley,

Drs. Nag, Suleiman, and Thomadsen, besides myself. And everybody had a piece of this patch to put into the Subcommittee report. So we will get to the specifics.

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

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

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

A couple of observations in using the NMED database, some suggestions for improvement. We thought these could be implemented, facilitate, and search capabilities, as well as being more certain of

capturing events. And that would be to do reports or queries by specific licensee type as well as also being able to use multiple key words. Right now you can only use one key word when doing searches in NMED.

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

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

Looking at the first category of 35.300 events, which are unsealed radiopharmaceuticals requiring a written directive, there were seven events. Six involved I-131. One involved Y-90. Five of those 131 events were sodium iodide in the treatment of thyroid therapy.

The type of errors and the subsequent actions reported by the licensee are indicated on this slide for the Y-90 and I-131 bexxar, which have similar types of clinical treatment purposes and a couple of the I-131s. And as you'll notice in this slide and in the next slide for the I-131 therapies,

the type of error was failure to follow the written directive.

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

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

Probably in the preamble to the Committee, this Committee report, I should mention this was the first time that we have actually had a formal Subcommittee report on medical events and that one of the things that we're trying to do is track trends so that as we do subsequent reports, we will continue to track the number of events that are reported and report back to the Committee for potential future

action.

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

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

If we look at the type of errors for the manual brachytherapy, we see that failure to identify positioning with ultrasound occurred in three of the events, prostate implants, and in the other was the patient movement and failure to reposition based on ultrasound imaging and then again the applicator malfunctions and the incorrect source strength being input into the treatment planning computer for the low-dose rate therapy.

The observations, the common issue with

prostate implants was improper identification of land boundaries by ultrasound, the observation being that, even though it's beyond the scope of the NRC, the need to assure adequate training and that imaging protocols have been established in the use of the ultrasound before the procedure.

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

The other observation, which relates to the source strength issue, was that orders both by the licensee and the manufacturer for radionuclide implants, specifically the seed implants, need to document both the air kerma strength as well as any other desired unit, whether it be a current activity or milligram radio milliequivalent. But it's the licensee responsibility for verifying that the proper unit is input into the computer entry. The recommendation here is that scientific societies consistently recommend that the standard of use of air

kerma strength be used and the need to reinforce this with manufacturers and users.

And there is in process right now a draft I believe it is information notice from the NRC that will address this specific point. So action is in progress.

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

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

The next category is category 35.600, which involved remote afterloaders in teletherapy. This was a breakdown for fiscal year 2007 versus 2006. There was only an increase of three medical events for all these uses.

Regarding all HDR, there was an increase by two, the medical events. The breakdown for the HDR because in the past, it had been broken down into MammoSite uses versus other HDR medical events, the Subcommittee further broke this down also into the use for vaginal cylinders, which had -- this was not reported in the previous medical event I guess I

should say summary that we did in the fall for 2006 events, but the Subcommittee felt that this was important to specify as a separate item because vaginal cylinder implants are usually considered the simplest, most standard type of HDR application for these types of devices.

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

There was one event involving LDR remote afterloaded and two with gammonite and none with other teletherapy devices.

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

What I think it means is that people who do HDR very infrequently only do vag cylinders. They don't go into the more complex one because it requires sedation or operating room and so forth.

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

MEMBER LIETO: Thank you.

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

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

Looking at the vaginal cylinder breakdown, you can see that the causes were wrong, step size wrong, isodose being selected, wrong catheter length being entered in the treatment planning, fluid in the source track, improper default length used.

So, again, the emphasis that the

Subcommittee wanted to indicate is that, even what is considered the most simplest treatment in the use of HDRs does result in a fair number of medical events overall in the use of HDR.

MEMBER VETTER: Could I ask a question?

MEMBER LIETO: Sure.

MEMBER VETTER: These data came from NMED.

MEMBER LIETO: Right.

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

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

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

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

MEMBER VETTER: No.

MEMBER WELSH: Separate?

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

MEMBER LIETO: The answer is no the best I

can tell. Debbie?

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

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

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

DR. HOWE: Not in NMED.

MEMBER GILLEY: Not in NRC regulations.

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

MEMBER NAG: Yes. They won't be because if there are minor errors, less than 20 percent, previously, as we said, 10 percent was a reportable event, and that information would have been filed.

But now it won't.

MEMBER VETTER: Correct.

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

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

MEMBER SCHWARZ: I have a question.

CHAIRMAN MALMUD: Yes?

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

MEMBER LIETO: Yes.

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

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

MEMBER THOMADSEN: Donna-Beth has --

CHAIRMAN MALMUD: Donna-Beth?

DR. HOWE: I just want to make an

additional comment. And that is that if there is something that is considered a device failure, then those are reported under 30.50 or part 21. And Ralph I believe discussed those in the October meeting.

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

CHAIRMAN MALMUD: Thank you.

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

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

Vaginal cylinder, surprisingly, dominated the number of events considering they're considered to be the more simpler type of events. To get to Dr. Schwarz's comment about do we have any statistics,

based on 2006 data, it's estimated that 32,000 patients were treated with 35.600 applications.

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

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

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

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

MEMBER VETTER: So six sigma would be way out.

MEMBER THOMADSEN: You may have heard in

industry, they deal with six sigma as trying to improve the quality. That's the goal as to get out that. Nobody makes it. Well, the airlines.

CHAIRMAN MALMUD: Well, the airlines do.

MEMBER THOMADSEN: Airlines.

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

Was your question answered?

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

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

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

However, because the outcomes are time-related, it is difficult to say with certainty

what the morbidity and mortality are. And, therefore, we are constantly working at improvement, as we all do every day, as you do in your practice and I do in mine.

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

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

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

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

MEMBER LIETO: And probably we also should point out the denominator for the fraction of this is 2006, although the fiscal year numbers and the numerator for 2007, the presumption is that the denominator is going to change that dramatically from 2006 to 2007.

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

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

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

CHAIRMAN MALMUD: Any questions for Mr. Lieto?

(No response.)

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

The fetal embryo dose is not under the definition of a medical event. And that's why it's under this other category. And then also included was other reportable medical events into the NMED that involved the medical use of radionuclides. There were 15 of these events.

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

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

The other 35 events were the 2 pregnant patients that were administered I-131 therapies. In the one event, the patient was 13 to 15 weeks pregnant and was administered 15 millicuries of sodium iodine. In the other, the patient was 4 to 5 weeks pregnant and was administered 125 millicuries. And the people dose estimates are as indicated in the NMED reports that are specified there.

In terms of other material events, there were the six events involving lost sources. Four of these events involved prostate seed implants that were lost. One case was a breast tumor localization. The

other three were after prostate implants.

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

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

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

In another event, the seeds, which is not I think a common practice, were leak tested before implant. And removal contamination was found four times that allowed for for removal contamination from a sealed source.

The other event involved contaminated

packaging. I would kind of lump this as one event, even though there were three incidents from the same licensee, shipments from a centralized pharmacy having surface contamination on the package being received above reportable limits. No cause was specified in these events.

And then the other miscellaneous, one was a teletherapy malfunction. And this was I think one of the events that Dr. Howe was referring to where the source stuck in the open position failed to retract.

Staff responded promptly based on training for emergency intervention, returned the source into a shielded event. And, as a result, the patient unexpected dose did not exceed 20 percent. But this would be reported not as a medical event but as an event under 35.50.

And then another on a sort of I'll say unique event involved a number of individuals who were given diagnostic agents involving chlorine-18 and technetium-99m for purposes of training employees and evaluating new imaging equipment. They exceeded the dose levels allowed for members of the general public. And, as a result, this was reported by the agreement state.

In summary here, listening the materials

events, comparing fiscal year 2006 versus 2007, we see a significant increase in the number of events being reported for the Y-90 under 35.1000, an increase on the embryo fetus dose. I guess you could say it doubled, even though it only increased from one to two.

The loss sources and leaking sources were fairly constant or decreased. And, as I mentioned, we lumped in the miscellaneous events of the contaminated package as a single event. So when you look at these miscellany events, they either decreased or were fairly constant.

Overall there were 19 events in fiscal year 2006 versus 25 for fiscal year 2007. Now, we wanted to try to trend this also to look at medical events over the last four years because in the NMED report, fourth quarterly report, there are statistics that indicate the number of events over a 16-quarter period.

When we looked at these, just summed these up into annual totals, as you can see, the medical events seem to be fairly constant over the four-year period. What we are maybe looking at is just the natural variance in an uncommon event that occurs over that time period.

The other thing we wanted to compare it to was also the medical abnormal occurrences that are reported. Now, an abnormal occurrence, which is going to be discussed a little bit later by Angela, are the most significant events, medical events, that occur. They have to be above a much higher threshold than required for medical events. And these events are reported to Congress on an annual basis. So these are sort of the most significant of the medical events.

Now, one of the things that I would like to indicate is that in the abnormal occurrences, this would include like not only the significant medical events but also the embryo fetus dose events. The medical events that are reported in the NMED report do not include in them events that involve the embryo fetus doses because they are not "considered medical events." So just kind of be aware of the differences in some of the numbers that go into that.

The abnormal occurrences might indicate that there is an increasing trend, but, again, this might just be a variation in a very small number of events that we're seeing over this time period.

Probably the final point that I wanted to make is that in terms of the medical events, it's not necessary that one medical event involves one patient.

So a single medical event could actually involve a single report of a number of patients. And I know that is the case in some instances regarding the brachytherapy seed medical events that have been reported in the past.

And I think that is the last slide. So the Subcommittee and I would be glad to entertain any questions.

CHAIRMAN MALMUD: Thank you, Mr. Lieto.

Are there any questions for Mr. Lieto or comments from other members of the Subcommittee?

MEMBER SULEIMAN: I have a question, clarification.

CHAIRMAN MALMUD: Excuse me.

MEMBER SULEIMAN: I don't know why I didn't ask it earlier, but the misuse of the radiopharmaceuticals for training purposes, who cares what the threshold is? That's just improper. There are regs that that is a violation of.

Donna-Beth? In other words, what if the doses were below 100 millirem? Who cares? What was done was inappropriate. It was unethical. I thought state --

MEMBER GILLEY: As part of the radiation protection program, they are required to keep doses as

reasonable as possible. We would take action. So I don't know what this particular state did, but it would be a failure to --

CHAIRMAN MALMUD: Donna-Beth?

MEMBER SULEIMAN: The trigger shouldn't be what they find. The sheer fact that they did that was incorrect.

CHAIRMAN MALMUD: Donna-Beth?

DR. HOWE: Generally we find out about these events because of allegations. And then we look at violations and we find it's not a medical event. And then we find out that we find some other violation that we can tag it to. And then we generally find out that it's willful.

So there is not, per se, a reporting requirement for this. We generally find it out after the fact through allegations. We do have a public --

MEMBER SULEIMAN: Would these really qualify as medical events or --

DR. HOWE: No.

MEMBER SULEIMAN: No.

DR. HOWE: No. And they're not reportable as medical events. And that's one reason we find out about them primarily through allegations.

MR. LEWIS: Just to be clear, if it had

been below the public dose limit. But these were above it and would be reportable under part 20.

MEMBER GILLEY: These were diagnostic. These were diagnostic bases.

MR. LEWIS: Diagnostic.

MEMBER GILLEY: They don't qualify.

MR. LEWIS: They were over 100 millirem?

MEMBER GILLEY: None of them were.

DR. HOWE: It's not the public dose limit because the public dose limit is the licensee is not supposed to have its problem so that it gives the member of the public an access. These are deliberate acts.

MEMBER SULEIMAN: Nonmedical use.

DR. HOWE: Nonmedical use.

MEMBER GILLEY: Or not the public. They're occupational workers. The standard is different.

DR. HOWE: But they're not permitted these doses under the normal occupational levels either. So we don't have a specific regulation that says, "You will not irradiate people." But we do get it through violations and allegations.

CHAIRMAN MALMUD: Dr. Eggli?

MEMBER EGGLI: Actually, though, I think

there is a specific regulation that says a dose administered has to be for medical use. So I don't remember exactly where it is, but I think it is out there that any radiopharmaceutical administered has to be for medical use.

CHAIRMAN MALMUD: It is. Mr. Eggli?

MEMBER GILLEY: It has to be all the data if there were a clinical procedure with a clinical procedures manual or it has to be a written order from an authorized user. Those are the two mechanisms. You either use a clinical procedures manual or you can use a --

CHAIRMAN MALMUD: I suspect that in our state, it is a violation of the Pharmacy Act because a radiopharmaceutical as a pharmaceutical requires a prescription. And these individuals would have been administered pharmaceuticals without permission, without prescriptions.

MEMBER EGGLI: And I think in some of the cases where you are looking at -- this is Eggli -- administrations for testing equipment, that first in most dose ranges, a written directive wouldn't be required, but in clinics where there is a practice to do a written directive, the written directive probably would have been written.

I think that there are a lot of practices out there who, in fact, don't understand that you can't administer radioactive materials just to test new equipment. You can sort of give away tests to people who have medical indication when you are testing new equipment, but you can't recruit folks, normal volunteers, without a research protocol.

And in most states, although it's not an NRC regulation, the same is true for CT or any form of ionizing radiation, that normal volunteers cannot be studied. But, yet, I think most end users are probably unaware of that.

CHAIRMAN MALMUD: Any other questions or comments? Yes, Mr. Lieto?

MEMBER LIETO: I just want to again thank my Subcommittee members for their support and aid.

CHAIRMAN MALMUD: Can you name them for us, please?

MEMBER LIETO: Yes, Debbie Gilley, Dr. Thomadsen, Dr. Suleiman, and Dr. Nag.

CHAIRMAN MALMUD: Thank you. That's for the record. Thank you.

And if that completes your report?

MEMBER LIETO: Yes. We have no recommendations for Committee action.

CHAIRMAN MALMUD: Thank you very much.

We will now move on to the next item on the agenda, which is "Causes of Medical Events." Dr. Thomadsen?

MEMBER THOMADSEN: You could just pass that along.

CHAIRMAN MALMUD: We are going to have a handout?

MEMBER THOMADSEN: Thank you.

7. CAUSES OF MEDICAL EVENTS

MEMBER THOMADSEN: One of the goals of my presentation is to discuss root causes of errors. And so we should start by looking at what is a root cause. To that, we should look at two divisions of failures that happen.

There are failures that are results of active errors; that is, something that somebody does. Somebody commits an act. And because of that, something bad happens. Then there are latent errors, which are the organizational or environmental conditions that lead an individual to fail.

Latent errors have certain characteristics. Active errors usually only affect the particular patient -- while that is what people say -- while latent errors can affect all the

patients.

This isn't really true. An active error, such as an incorrect calibration from a machine, could affect a large number of patients while a latent error might only lead to an event that injures one or maybe never anybody.

Most often, though, it is true that active errors are a one-time, one-patient thing and latent errors are systemic errors, which form traps that people fall into. And that leads people to make an active error. Latent errors often are things like lack of staffing or the policies or training practices.

Usually you would like to do a root cause analysis of events and find latent errors because that way you could fix the system. They are often very hard to find.

Also you often find that latent errors are things that are very hard to change. They are built into the organizational structure as a large hierarchy. And that is not likely to change or their attitudes in the administration, which are not going to change.

But you would like to find latent errors if you can because that way you might be able to

change something that might lead to a lot of different errors. And fixing the latent errors, however, is not necessary to fix the problem. And we'll get to that in just a little bit.

If we're doing an event analysis, very often we'll start with a process tree or a process map that helps understand the process. And then we do an FMEA that is a failure modern event analysis. But when we're setting up our process, we understand what could happen and try to prevent that.

And, just like we have the process tree when we're setting up a process in the first place, although most people don't go through that, after there is an event, we do an event analysis diagram just to help us understand the event. That is all it is for.

The diagram is often built by a team, which can take a long time with a lot of arguing, and people disagree or sometimes it is done by an individual, which leads to the problem that the individual may not understand parts of the event or misinterprets something.

As I say, the main tool in the root cause analysis is a root cause analysis tree, an RCA tree, or diagram, which starts at the top with the event at

the top of the box. And then you ask, what actions immediately preceded the event? What caused it right at that moment? And these actions are boxes just below the event, usually going by a fault tree.

So here is an example of a fault tree where somebody fell down the stairs. And cause, the immediate cause, was that person was carrying laundry and couldn't see that there was a cat sitting on top of the stairs. And so you have two immediate causes.

If you took away either of those causes, you would not have had the event, which is why they go into an entry. Both causes had to be there simultaneously or the event wouldn't have happened. If you took away one of them, you interrupt the propagation of the error, which either one of those could be.

Immediate causes are called the proximal causes. For each proximal cause, you go around. And you ask, well, what caused that? And you keep asking, "What caused that?" as you build the tree. And you keep going down until you get to the last action over which you had control.

The causes for that last action, being out of your control, are of no interest to you. So you define that as your universe. You stop asking the

questions after you get to the point where you no longer have control.

For an example, to try and define where the edge of the universe is, if the power utility has an outage and in the hospital, the surgeon in the dark cut off the patient's head, you don't care why the power utility lost power. You couldn't affect that if you wanted to. So you stop asking at that point. That is outside of your universe.

You do care what actions take place in the hospital that led to the surgeon cutting off the patient's head. That is within your range of control. So your universe is drawn where you can have control over things and you can't.

Progenitor causes are those things at the beginning of each of those paths, the first thing inside of your universe that led to the pathway that eventually caused the event. The progenitor cause may be a root cause or it may just be a condition.

An example of a condition would be the primary nurse who was supposed to be taking care of something was home sick. There isn't anything you could or would do about that. That's not a cause per se. It is a cause, but it is not a cause that you are interested in. So it is not a root cause or in our

simple example, the cat sitting on the top of the stairs was just a condition.

And it's not something that you necessarily will do something about. I suppose if you change your cat, then the cat wouldn't have been there.

In the diagrams, often progenitor causes are shown as ovals.

We want to find root causes, but the whole concept of root causes is not clear. It sounds wonderful, and it sounds like something you would want to do.

What we're looking for with root causes probably are those things that you can change that would prevent events of a similar nature. You would like them to be latent errors; that is, situations in the organization that facilitate failure initiation and propagation. You often find active errors; that is, something somebody did.

The very fact that most of the time we've got these and gates implies that there is no root cause. There is no one thing that caused anything. You had to have a set of conditions.

The environment is often a contributing factor. And that enters the tree from the side,

through a diamond, just sort of like a transistor. Here we have a cat sitting at the top of the stairs. There is an environmental condition that the light was low. And so somebody tripped over the cat. That is not so much seen as a cause as a condition. But we will see that those types of conditions need to be fixed right away.

What do you do? Sometimes a progenitor cause is a truly latent cause but may be too hard to fix. But one shouldn't worry about that because to prevent the events, all you need to do is set up something that will interrupt the propagation of a failure. You don't have to cure all the problems. All you have to do is set up systems that will interrupt the flow.

This is a rather famous illustration from James Reason's book *Human Error* that is shown in almost all talks on error propagation, showing that you've got all sorts of levels of defense in any system that you have, any organization, where you try to prevent things from happening. But almost all defenses have holes in them. And if all the holes happen to line up, then you can have the event propagate right through it.

Of course, what you need, you need to have

the event be initiated at the beginning, and you have to have these holes all line up. So it's a complex situation that very rarely happens, but it does happen. And this is what you try to prevent.

You can prevent the error by looking at the beginning or by just changing any of those defenses so you no longer have the holes line up.

This except it's gone off the bottom is an example of a root cause analysis tree just showing they do get somewhat complex. You see it starts at the top.

We are joined by an and gate. Almost every root cause analysis I've ever seen has an and gate right under the event. Humans are one deductive and can handle something that goes wrong.

The problem is when something goes wrong and something else goes wrong. When we have got two things happening at once, then it is a problem. And that's when events actually happen.

And you can see that each event on the left side as you go down has an and gate right after it because, once again, each of those steps probably by themselves could be handled quite well by anybody. But when you put them together with other things, people have problems.

The difference you can almost see, you can't see in your slides, in your book but on the screen, you can maybe make out. But at the bottom, some of those ovals because the progenitor events are a darker yellow and some are a lighter yellow. The light yellows are those that are just conditions, and the darker yellow are actually progenitor causes that you could do something about, that you might be able to fix.

The small text -- I'm not expecting you to read any of these. And, particularly on the handout, you can't read anything. But the small black text off to the side of some of the boxes is looking at what the classification of those boxes would be, those failures in the boxes, if you were looking at them with certain taxonomies, which are useful for trying to classify types of errors.

This is just another one. It's easier to see in your book than on the screen, where the color black gets blended in with the dark blue. But those arrows are pointing to where a cause actually feeds into two sides of a tree.

And usually when we're looking at these trees, if you've got an and gate, that actually means you had different levels of defense where you had the

failure. And, in general, you probably would be fairly good.

Here when you've got a cause that feeds into two sides of the tree, that means that you actually are doubling the likelihood that something would go wrong. And that's a real hazard when you analyze these things.

If we look at what to do, all failures actually are system errors because the system didn't prevent the propagation of the error. So, even if the causes are active errors where somebody did something, the system should be set up to be robust against that and interrupt the propagation of the error.

All failures are human errors because somebody did something wrong. And all the latent errors are human errors because somebody made a bad decision somewhere.

If you had, as I talked about earlier, a machine calibration where you injured a lot of patients, that was a systemic error. But it was an individual who did it. So it is an active error also.

So even the definitions of latent errors, active errors, system errors, and sporadic errors are very interrelated. It depends how you're looking at them as to what the definitions actually mean.

Latent errors, as I have mentioned several times, are usually very hard to fix. They are often, as I say, like trying to make somebody change their religion. They are built into the operations of your organization.

The prevention of similar events can be done by either eliminating the progenitor causes or by interrupting the propagation. Often the interruption is much easier to do.

If you look at this, are root causes always latent errors? No, they are not. Are root causes always progenitor causes? Actually, no. No, they aren't. Are progenitor causes root causes? Absolutely not.

For an event where a dosimetrist entered the wrong dose, the root cause is not that the dosimetrist entered the wrong dost. That's just part of the event. And if we look at NMED and try to call out from NMED what is the root cause, unfortunately, you often see this type of inscription. The cause of the event is the dosimetrist entered the wrong dose.

The root cause, if there is any such thing, is why the dosimetrist entered the wrong dose and why such an entry propagated to the patient. Those are the questions. And the root cause is

somewhere underneath there.

Patient intervention is never a root cause. If we see that in an event, that is not considered a real event because there was patient intervention. That is not a viable explanation because why. Why does the system allow something, an untrained patient, and do that will propagate into an error? Why don't you have something set up to prevent?

A common example if you look into the bronchial treatments, it will be that the event is that are reported often is the patient has pulled out the catheter. Why is the catheter not sutured in place? Why is it not taped better? Why don't you watch the patient better?

NMED reports almost never give enough information to actually determine the causes, almost never give an indication of whether the corrective action is likely to work, which is a whole other discussion. They do give the model number and strength of the sort, which is usually pretty irrelevant to the discussion at hand.

If we look at error-preventing techniques, this is information from the Institute for Safe Medical Practices. There are different levels of how

effective a remedial action could be. The most effective are the forcing functions up at the upper left; that is, interlocked barriers, computers with feedback, followed by automation and computerization, bar codes, monitoring. Protocols are a big cut down on there. Check sheets and alarms, they're good. They aren't anywhere near like forcing functions. Redundant checks come at the next level. Rules and policies are pretty near the bottom. And at the bottom is education. Particularly of interest, we will see in reports of events, remedial action is to train individuals.

The last thing, before I go to the next slide, environments always should be corrected. I think the next slide, policies that don't or things that don't work. Policies usually are not an effective way to correct things. They're the most common thing you see. Particularly at my hospital, if there is a problem, the first thing they have to do is write a new policy.

Retraining. This is the education that we were just talking about. If there was initial training, if people were trained, retraining them never does anything. They know what they are to do. They know what they are to do.

There was an editorial in the newspaper back when there were civilians who were shot in Iraq. The military's response was to retrain people. And the editorial was it isn't that these people didn't know better. It's that they didn't do that and likewise in our events. The problem is people didn't. It isn't that they didn't know. All of these people knew. They just didn't do what they were supposed to do.

Supervision. Adding supervision to the job doesn't work. Expecting physicians to do more than check the client, despite the fact that they are the authorized users, they really don't know very much about what is going on. And any type of remedial action placing burdens on them is not effective.

Having people pay more attention, that's the least effective of these things. That does not work. Interestingly, the survey a few years ago amongst physicians as to what is the most effective way to prevent errors, 48 percent of the physicians, 48 percent of the different options they were given, said physicians have to pay more attention. I don't know if they are assuming they aren't paying attention now.

That is the end of the talk for now.

Another talk for the future -- actually, I see from the billing that I got on the table that Ashley went over this morning we are to talk about what things should be in the NMED database. And, actually, I was given a half-hour. That would be about another half-hour talk to look at what would be useful as far as classifications.

I think questions? Subir?

MEMBER NAG: You think that would work?

MEMBER THOMADSEN: Yes.

MEMBER NAG: How about saying, what do you think are things that will work that way? And then I'll go to the next comment. Do you have anything?

MEMBER THOMADSEN: Yes. The things that would work are essentially we have lost data. That was on the previous slide the priority error prevention technique, the institute of safe medical practice. Forcing functions, setting up systems that somebody just can do something wrong. If you have it interlocked, if you have a barrier that they can't get through, they aren't going to make those mistakes.

There's a big jump when you get to bar codes because there has been a whole slew of medical events, medication events with systems that use bar codes because what nurses have done -- and you have to

build a forcing function into the bar codes to make them safe -- is when they have the doors open, they pull out extra medications that they think they are going to need during the day so they don't have to go back and do all the bar coding.

So forcing functions are the most effective. That is what works the best.

MEMBER NAG: The other comment is from a practical standpoint -- I know you give more of a scientific slant. From a practical perspective, what I have found looking at my own practice and others around the country that I review, the one thing is that those who were doing a lot of the same kind of practice, I have found less errors or less abnormal occurrence in those practices. So repetition minimizes the error.

I don't know how to incorporate that in there. But that from a practical standpoint is very, very effective.

MEMBER THOMADSEN: Yes. On the paper that is copied after the slides, when we looked at brachytherapy events during the period, whatever the period was, one of the things we found, which was not a surprise at all, is new procedures are dangerous. That is when you have things going on with people who

aren't used to what they are doing.

We found that, interestingly, what would make a new procedure was not only that it was new somewhere. It could be somebody who has done this many times at a different hospital, moves to another hospital.

It was the first time at that hospital. Actually, the first time isn't always the most dangerous because everybody is watching like a hawk -- it is the second or third -- or it can be a hospital that has done the procedure a lot and there is a new physician coming to do it.

And the other thing the handout with the Joint Commission points out is an incredibly dangerous time when somebody is doing a procedure and passes the patient off to somebody else, in which case that patient is new to somebody who wasn't there for the end of it.

Oh, yes, absolutely. The unfamiliarity is terrible.

CHAIRMAN MALMUD: Thank you.

Dr. Vetter?

MEMBER VETTER: I don't know if it's safe to assume, but --

MEMBER THOMADSEN: It's probably never

save to assume.

MEMBER VETTER: Right, right. But many or some of these medical events may have been reported as sentinel events within the hospital, in which case the Joint Commission requires that a root cause analysis be done. I don't know if we can get plugged into that or if we can get information from Joint Commission, but we might be able to learn.

MEMBER THOMADSEN: No.

MEMBER VETTER: We can't?

MEMBER THOMADSEN: You cannot. And that is thanks to Congress. You cannot get that information. And the hospital cannot give it to you because of confidential peer review. And the reason for that is it's felt that if they don't close the possibility that word and details can get out, that people won't be so forthcoming in freely talking about what happens during the event for the root cause analysis team to be able to do their work.

You say, well, they don't have to pass the names, but chances are if you have an event at an institution and you describe what goes on and physicians talk, you can figure out who is involved.

So, instead, to allow the root cause analysis teams to do their work, Congress has said

this is all closed and the hospital cannot share that information.

It's made a real problem for compliance with the Joint Commission. The Joint Commission has found compliance with a requirement for reporting the sentinel events is very poor.

CHAIRMAN MALMUD: Thank you.

The effectiveness of double checking is probably the most effective technique, right, when you have two individuals with the same responsibility and one --

MEMBER NAG: No.

CHAIRMAN MALMUD: -- must check and the other must check off at the same time?

MEMBER THOMADSEN: It depends how you've done that. There have been studies that have shown this, too. For example, if you have a form the person checking has to fill in, you need to have two blanks for everything that goes on that form: one blank for what they find and one blank for what they expect to find. That is, you have to write down what you expect as far as dose, for example, and what you actually see on the plan. If you don't do that, it's too easy just to write down what you expect and not actually see that there is a difference.

Also, if the person reviewing checks a box and says, "I've checked the dose," that has almost no value as far as a second review. I mean, there is a great deal of science that goes into sculpting this type of quality management.

CHAIRMAN MALMUD: Dr. Fisher?

MEMBER FISHER: If one person knows that another person will be checking his results, that person is more highly motivated to be careful in the first analysis.

MEMBER THOMADSEN: That is true.

MEMBER FISHER: Thank you.

CHAIRMAN MALMUD: Dr. Nag?

MEMBER NAG: Again, this is a personal observation from practical experience. What I have found is that many of the so-called operator errors or errors occur under pressure when you are trying to do something quickly, which usually happens when a patient is on the table when you are about to give the treatment.

And what I have found is if you had a dummy treatment plan already done where you had something similar for the plan and then you are then doing another plan, which would be altered because of circumstances on the table and then you check on your

original plan and if it's not too far, then the chances of having a big error are small.

So there are errors and errors. You can have small errors of one percent, two percent, which are not clinically relevant to the patient and not helpful. And you can have a big error. And usually big errors tend to occur when you are in a rush or you have nothing to compare it against. And that would always include to have a backup plan ready or a dummy plan similar to what you are going to do.

So, I mean, if we can get some word out if my portion is we do that to the people, but if we can from ACMUI have something like that, that would be helpful to the community.

CHAIRMAN MALMUD: Thank you.

MEMBER GILLEY: Debbie Gilley,

You didn't consider the work environment in your root cause analysis or is it covered under another name?

MEMBER THOMADSEN: That was covered under environment.

MEMBER GILLEY: That's environment?

MEMBER THOMADSEN: Just environment. Certainly that is very important.

MEMBER GILLEY: There is a cooperative

spirit amongst physicians, therapist, dosimetrists if this is very important calling through those things.

CHAIRMAN MALMUD: Thank you.

If we may, then, we will go on to the next item on the agenda, which is Angela McIntosh, "Potential Revision to AO Criteria." It's Angela and staff.

MS. TULL: Actually, I have a revised agenda. You may have one in your binder to have all of the names of everyone and the correct times.

CHAIRMAN MALMUD: That includes P. Lanzisera and S. Gabriel.

8. POTENTIAL REVISION TO AO CRITERIA

MS. McINTOSH: Good afternoon. Our presentation is on the future revision to the abnormal occurrence criteria. Let's begin with a definition of what an abnormal occurrence is. It is an unscheduled incident or event that the NRC determines to be significant from the standpoint of public health and safety.

The purpose of reporting abnormal occurrences is to keep our stakeholders informed that they are occurring, our stakeholders being mainly the U.S. Congress and the general public, such as industry, well, you know, industry and the general

public, I should say.

And abnormal occurrence reporting is required. It's a law. It's not something that's done arbitrarily. We do have to report these things in accordance with the Federal Reports Elimination Sunset Act of 1995.

We recently revised the abnormal occurrence criteria. Back in October of 2006, we published the revised criteria in the Federal Register. We revised the criteria for two main purposes, the first being to make sure that the criteria are consistent with our strategic plan for fiscal years 2004 to 2009 but also to make the criteria consistent with the 2005 NRC rulemaking on 10 CFR Part 35.

Now, to explain briefly what the current criteria are, what we have here on the slide, on the following slides, are redline strikeouts to show you what the changes were, but these are the current criteria.

So right there you see that there was a change to the dose to the gonads, that first criterion equal to or greater than 100 rad to a major portion of the bone marrow, et cetera, or greater than 250 rad or 2.5 gray to the gonads or -- all these emphases are

mine -- equal to or greater than 1,000 rad to any other organ or tissue. So either one of those criterion plus either A or B would make an event become an abnormal occurrence.

Now, the process to revise the abnormal occurrence criteria is similar to rulemaking. We have to submit the criteria for public comment and get the criteria published in the Federal Register. So in terms of the resources that it takes for us to put out new abnormal occurrence, it's similar to a rulemaking.

So, in other words, it's a significant undertaking to change the abnormal occurrence criteria. That's one of the reasons why we wanted to bring the proposed revision to you to get ACMUI's input and possible recommendations about what we are proposing because it is a pretty significant resource impact for us to change these criteria.

With that --

MS. GABRIEL: I'm Sandy Gabriel from Region I. And I am going to briefly talk about an informal review that Region I staff recently performed to determined if all brachytherapy events meeting the abnormal occurrence criteria are expected to result in significant adverse health effects to the patients.

We went through and met reports of

brachytherapy medical events for fiscal year 2007 as well as the draft of the 2007 abnormal occurrence reports to Congress.

We identified a number of events that appeared to meet the abnormal occurrence criteria, whether or not they were actually reported as AOs, for which the medical consultant concluded that no significant adverse health effect is expected.

We also identified some similar events for which there was no medical consultant. These were agreement state events where a medical consultant wasn't required. That might similarly result in the same conclusion of no significant health effect.

This slide shows four events in which permanent prostate implants were displaced from the intended position. All four involved an underdose to the treatment site.

And it should be noted that underdoses are not reportable as abnormal occurrences. But because the implants were displaced, there was an overdose to unintended tissue considered to be a wrong treatment site, which would meet the second criteria that Angela presented a minute ago.

I was the inspector for the third event on this list: The New Jersey event. And in this case, a

medical consultant did review the case and concluded that no significant adverse health effect is expected. The other three cases represent similar circumstances.

The next slide shows four additional events in which temporary implants this time, rather than permanent, were displaced from the intended position. The first on the list was a tandem and ovoid manual brachytherapy treatment. And the three remaining items on the list were HDR treatments.

Again, all events involved an underdose to the treatment site as well as an underdose to unintended tissue, which would be considered the wrong treatment site.

I was the inspector for the Virginia event shown at the top of this slide. And in this case, which was a tandem and ovoid treatment, the sources in the two ovoid applicators were accurately positioned. However, the tandem insert that was used was four centimeters too short.

So the tandem sources were displaced by four centimeters. This caused an underdose to the cervix, which was a treatment site, and overdoses to very small volumes of adjacent tissue. Again, a medical consultant reviewed this case and concluded

that no significant adverse health effect is expected.

The next slide shows two additional types of events that may not result in significant adverse health effects. The first is an HDR treatment with fractionation different than was intended. And the second is a liver microsphere treatment that resulted in inadvertent dose to the patient's gallbladder.

Now, Penny from Region I is going to speak about possible revisions to the AO criteria.

MS. LANZISERA: As Sandy just noted, for many of the brachytherapy cases, the NRC medical consultant concluded that no significant adverse health effects occurred.

So the following questions came to mind, and they are represented here. Should the NRC criteria focus on significant health effects only? Should reporting for wrong radiopharmaceutical, wrong root, wrong treatment site, or noted on individual source be removed from the current reporting criteria?

So based on this review drafted for discussion today that are summarized at the end of the presentation with the actual language along with the current AO criteria, the first option that we have here, "Remove the organ and tissue dose criteria and introduce similar concepts," the concept that the dose

that occurred is unintended is the first concept introduced.

Additionally, we have permanent functional damage or significant adverse health effects represented in the --

(Whereupon, the foregoing matter went off the record briefly.)

MS. LANZISERA: Again, the permanent function, damage, or significant adverse health effect is added. And this damage would be damage that wouldn't have been expected from the treatment regimen.

And what we were thinking here is that this would include the entire patient treatment, brachytherapy along with external beam and any other component of the treatment.

The second option retains the 1,000 rad organ tissue dose that is in the current AO criteria and adds the new concept that links this 1,000 rad to the doses greater than the dose expected during the treatment regimen and is done as the patient's entire treatment, which means for the external beam as well.

The third option is similar to option 2 but contains also the concept of the 50 percent greater than described as in the current abnormal

occurrence criteria.

And then the fourth option takes the language for abnormal occurrence from the Federal Register notice, which is "a significant impact on patient health that is likely to generate high public interest," and links that to that this significance is determined by an NRC consultant physician.

All of the options provided lead to the concepts of the wrong root, wrong treatment, wrong pharmaceutical. Again, you had that one in your enclosures.

CHAIRMAN MALMUD: All right. Does that complete your --

MS. LANZISERA: Yes.

CHAIRMAN MALMUD: Thank you,

Discussion? Dr. Vetter?

MEMBER VETTER: Angela, you said that this will involve a lot of effort?

MS. McINTOSH: Yes.

MEMBER VETTER: And how many events are we talking about affecting here? How many fewer events? If we made one of these changes, how many fewer abnormal occurrences would there have been in this past year?

MS. McINTOSH: Probably would have dropped

the number near to zero if not zero.

MS. LANZISERA: You'd still have your abnormal occurrence ones for the embryo fetus for those types of events, but all of the prostate ones that are current that are in the current one would go away.

MEMBER VETTER: So you think it's worth making the change?

MS. McINTOSH: We think that it would.

MS. GABRIEL: Yes.

MS. McINTOSH: In a word, yes.

MR. LEWIS: Part of the problem I think is that in the rest of the agency, where all the abnormal occurrences result in inadvertent exposure, it is a really big deal to Congress. Our definition of medical sweeps in a lot of things that maybe Congress doesn't need to know about and when they tell us, they will tell us.

But backing off to put these events in the same tier as the other abnormal occurrences that happen in the agency is really unfair.

CHAIRMAN MALMUD: Debbie Gilley?

MEMBER GILLEY: Yes. I noticed that you used consulting physicians to make the determination of the medical impact to the patient. Not all

agreement states do that. Is that a standard for NRC to always use a consulting medical physician?

MS. LANZISERA: Yes. It's part of our policy that we offer any medical --

MS. GABRIEL: In certain circumstances.

MEMBER GILLEY: So you do have some flexibility as to when you would call a physician in to give an opinion of whether or not there are adverse effects to the patient?

MS. GABRIEL: We always have the option to do it. And our procedures dictate that in certain circumstances we are required to do it.

MEMBER GILLEY: Okay.

CHAIRMAN MALMUD: There's another question.

MEMBER NAG: I think it definitely is important to have the medical consultant's opinion because I have been a medical consultant on many of these cases. And many of them are from a medical standpoint very insignificant.

Legally yes, they are errors or they are abnormal events or medical events, but they are not of any consequence to the patient, especially these patients would get the external beam.

Many of that area would have to radiate

much more than that just from that inner beam portion. They directly proportionate a little more dose to that area, which is technically a medical event but to going to affect the patient.

So I think it is very important that we separate out things that are going to be a flat thing that the Congress and others need to know about, which is others that really report it and which is important to improve our performance but not necessarily needed to let the entire population be fearful of it.

CHAIRMAN MALMUD: Dr. Thomadsen?

MEMBER THOMADSEN: Thomadsen.

I have my doubts about much of the data upon which you are basing these recommendations. For example, in Kansas, the event for a MammoSite, the implant was just placed 2 centimeters, resulting in 100 gray to an unintended site.

I've seen many of these accidents. And they actually do have considerable effect on the patient. Particularly in that case, at best, I would have a considerable amount of fat necrosis on the side that was overdosed.

And while you don't consider underdose an event, you have half of the target volume receiving essentially nothing therapeutic, which true for a

breast case, probably for a MammoSite case, in particular, the women may not have needed radiation in the first place. But if we assume that we are giving radiation for some reason, underdoses are deadly.

In looking at some of the other ones, the medical consultant may have been privy to particular information, but their estimation of the biological effect of the patients are certainly understated.

If that is not the case, if that is not the case, then certainly we should along with this change issue a guidance that quality management is no longer important in the medical use of radionuclides since none of these seem to imply that what we do makes andy difference whatsoever would simply our tasks as well.

CHAIRMAN MALMUD: Well, that's a stimulating statement.

(Laughter.)

CHAIRMAN MALMUD: Who wishes to respond to it? Mr. Lieto?

MEMBER LIETO: What we're talking about here is sort of a special category of medical events. The medical event is still going to get reported. You know, I am not going to question the judgment of the medical consultant in these ten events, but I am

going to just assume that based on their judgment, I support what NRC staff is trying to do here.

You know, I am going to look to my colleague in the corner over here, Dr. Suleiman, in that I know FDA has sort of a two-tiered reporting level for medical device problems, anything that causes contoured effect or unexpected effect to a patient. And then there is sort of the -- I don't know the name right off the hand.

MEMBER SULEIMAN: One is adverse event, and one is serious adverse event.

MEMBER LIETO: Okay.

MEMBER SULEIMAN: Seriously basically is potentially life-threatening or whatever. It doesn't define it any more clearly than that.

MEMBER LIETO: And I think that is kind of what is being attempted here, is to try to come up with what we report to the Congress and the general public in the Federal Register shouldn't be these events that are maybe below the serious adverse level and only not that -- I mean, it is still going to be reported.

And they still may be addressed by a committee such as ourselves or whatever, but if we are going to take this to Congress, we obviously are

indicating these are really, really bad things or undesirable things and should be sort of at the second level of reporting.

And maybe what we need to do is come up with addressing along that line. I think that is what these thresholds are attempting to achieve.

My concern is only that some of these are very soft terminology, like "expected" and "unlikely." I don't know if we want anything more specific than that, but I support the staff's intent to really only present the events that are determined to be of significant adverse effect.

MEMBER SULEIMAN: I'm conflicted. I defer to the oncologists on the Committee because I am surrounded by oncologists at the agency. And my perspective has changed because some of these products are used for cancer patients. Some of them are used for humanitarian or refractory purposes.

That means basically that these patients are extremely ill and don't have a very long life expectancy. And so treatment of that cancer may require some skill. And medicine, in some cases, it's less the science and more the art.

So where you draw the line in some of these quantitative, you know, 50 percent, 25 percent,

I am conflicted with the term "error." I think there is a baseline uncertainty. You just have a certain level of imprecision in delivering the therapeutic dose. I think that's just the state of the practice.

You know, is it one percent? Is it five percent? Is it ten percent? We tend to look at the numbers and think they are all the same. So I think it would require a little bit more thinking through.

I can't give you a straight answer or an opinion, but, I mean, I would be very, very hesitant to call a dose that a prescribing physician decided, you know, "This patient is pretty ill. Let's giving him something a little bit" -- you're not sure what amount of dose you want to prescribe.

And some of these are new procedures. So you're still learning. So I would be very, very careful about one quantitative change fits all sizes.

CHAIRMAN MALMUD: Dr. Welsh?

MEMBER WELSH: I'd like to look at this from a big picture perspective and ask, what is the goal of possibly changing things here or revising things? And one answer that I heard posed was that we should be asking, what do Congress and stakeholders really want to be informed about? How important are these things?

I don't want to question the judgment of the medical consultant, but, as Dr. Thomadsen pointed out, there could be some effects. And you would expect some effects from the cases that are listed here. But are they defined as significant adverse effects?

These gentlemen who have received dose to the penile bulb would probably have erectile dysfunction. Does Congress need to know about that? Probably not.

So the important point is, what is the definition of an adverse effect? And how can we make sure that we are quantitative in defining this so that we can be confident that things that don't have to go to Congress don't wind up going there?

CHAIRMAN MALMUD: Dr. Nag?

MEMBER NAG: I would also like to state that there is a wide range of diverse opinion in different treatments. And let's say if you are giving a drug by weight and you are allowing 20-30 percent difference or you are giving medication that absorbs at different levels in different parts of the body and then you are comparing that with brachytherapy and you are holding brachytherapy to such strength that if it is 21 percent more to an area that you are not even

sure of. You are not sure where the packet is.

And you are arbitrarily saying, "This is the target, and you are getting 21 percent more through this area." And that is an abnormal event, and you call that an abnormal occurrence. Then you are really holding to very inconsistent standards.

I think that at least having a physician making that determination is helpful, that was this error or was this deviation of significant proportion that the public at large needs to know about.

I know in chemotherapy, very often if you feel the patient is sick, you go down by 50 percent or 70 percent of the dose. And that is even advisable; whereas, in brachytherapy, the whole thing is very strict.

Just because it is under the definition of a medical event, that does not necessarily mean that there has to be a big alert. Yes, we need to know about this. Yes, we need to see how we can collect it.

CHAIRMAN MALMUD: Dr. Eggli?

MEMBER EGGLI: My comment sort of sits at a 50,000-foot level because I don't know enough about this to talk in detail. But usually that doesn't stop me.

It seems that the intent here, the key part of this is the expected-to-result permanent functional damage and that the intent is to reduce the reporting of events that don't have severe consequences.

Now, you can take the minimalist approach and just use that, but then nobody really knows where to start thinking about is this causing damage or what should be the threshold events that I might want to evaluate.

So from that point of view, I actually like option 3 best because everything else is trumped by what now is to be in option 3. If it doesn't hit that threshold, since there is "and" there, if it doesn't hit that threshold, it is not reportable but having in the other items sort of list what other things you might want to think about as maybe pushing you to the threshold where you might have significant damage in part 2.B.

So if you take option 1, you know, why is 101 gray to the bone marrow or 2.5 gray to the gonads more important to leave in as a specific reference than 10 gray to other organs or tissues or 50 percent over dose prescribed? You know, what makes one of these criteria more important to sort of raise or

sensitize people with?

So it makes sense to me that if the 2.B threshold trumps everything else, which is that there is no other tissue damage, then what you are doing here is listening conditions that you want people to think about as maybe causing significant damage and maybe ought to be triggers for evaluation.

So I would use option 3. If your point here was to get advice, that is one person's opinion.

MEMBER WELSH: May I comment on that?

CHAIRMAN MALMUD: Please do.

MEMBER WELSH: When I was bringing up the point earlier about quantitation, it is sort of a rhetorical question because significant injury -- is that 50 percent risk of injury, 100 percent? There's no definition.

If we had to make up a definition, I think we would all come up with something slightly different in terms of what number of sieverts or gray would reach the 50 percent threshold. That's why I like option 4, because it's the only one that's not put in numbers.

And if we are going to stick to something quantitative and defined, it is going to be difficult. Death is easily defined. And number two might be a

little bit more subjective, but still it avoids the issues of numbers.

CHAIRMAN MALMUD: Thank you.

Dr. Eggli?

MEMBER EGGLI: What I don't like in option 4 is who is deciding what is public interest? Is it Geraldo or Oprah? You know, who is deciding what is of significant public interest here? That is going to the sensationalists are going to find everything of significant public interest. And what is the definition of significant public interest?

So that part of number 4 I don't like at all, actually.

CHAIRMAN MALMUD: Mr. Lieto?

MEMBER LIETO: As a compromise, could we move 2.B in option 3 into 2 of option 4? Would that make sense?

MEMBER THOMADSEN: Actually, if you do that, you don't need option 1 in number 4 because I think 1, the death, could be considered a permanent function.

(Laughter.)

MEMBER LIETO: I would accept that modification.

MEMBER GILLEY: Definitions of these two

to assist in determining whether there have been significant adverse health effects. Is NRC prepared to do a definition for those things?

MEMBER VETTER: Coming from the physics side that would have to measure things, I would vote for option 3. The option 4 is just so subjective for me it's hard to get my hands around it.

MR. LEWIS: What I think is not subjective about option 4 is in the opinion of the medical consultant. So it always comes back to that one person's opinion is what we would decide to send down.

And if it's option 3, number 2.B, it doesn't have that. So I think it also answers Debbie's question. It's a medical consultant's opinion that was the defining criteria in that option.

MEMBER GILLEY: Is it then implied that we will need to have a medical consultant every time there is a medical event to give a recommendation? Because that is additional --

MR. LEWIS: Significant.

CHAIRMAN MALMUD: Dr. Fisher?

MEMBER FISHER: Darrel Fisher.

From a patient perspective, there really are only two considerations that are important, I think. One, was the proper treatment delivered that

would result in a beneficial therapeutic effect? And, two, was an improper delivery of radiation avoided that could result in some permanent dysfunction or adverse effect? Whether it's 990 or 1,050 is irrelevant to the patient. I mean, there is no magic number that says above 1,000, you have a significant event. Below 1,000, you don't have.

And so I think the important concept here would be not so much whether Congress thinks it is a significant event or the news media but, rather, did the patient receive the proper dose to the target tissue? And doses to normal tissues should not have been irradiated, were they avoided? I think it is as simple as that.

MS. McINTOSH: Can I respond to that?

CHAIRMAN MALMUD: Yes. Angela?

MS. McINTOSH: I think we agree that always important is the patient perspective on what has occurred. It's their body. And we should always be sensitive to that. But with these criteria, we are required to report certain things to Congress. And that is built into the whole reason for why we are doing this.

And so the criteria were initially developed from, actually, the reactor side of the

house from events that would occur in the reactor realm that Congress might be interested in knowing and the public might be interested in knowing.

And the medical materials side of the house has sort of come in after the fact, for lack of a better term, and been sort of retrofitted into something that was created in the reactor realm.

And from our perspective, what this has done, it has created a situation where the significant reactor events Congress is aware of, but the commensurate medical events are not really as significant.

And so we don't want to ever disregard the importance of keeping the patients involved about their own treatment and issues with their own medical treatment. But we just want to elevate the medical events so that there is an equivalency in significant adverse impact that has happened on the medical side of the house.

We currently think that that equivalence just doesn't exist. And so that is what we are trying to correct and not inform Congress of every little -- you know, pardon the expression -- little by comparison, relatively speaking, little medical event so that they are not just inundated with things that

really from their standpoint, it just isn't significant.

CHAIRMAN MALMUD: Thank you.

Dr. Suleiman?

MEMBER SULEIMAN: I mean, FDA does have a severe adverse event reporting system. And things sometimes happen out of the ordinary. I think what I do like in the wording of some of these is that, I mean, side effects, some of these medical products have some very serious side effects.

And I guess I can reconcile the physician's right to prescribe a dose, even though those prescribed doses may vary a lot. That is tolerable under the practice of medicine.

But once they have made up their mind, they are going to deliver such and such amount of activity or whatever. And if something happens where the patient gets much, much more than that, death results or whatever, the purpose of these regs is to sort of identify these outliers.

So I think conceptually you are right. The problem is how do you calibrate the abnormal occurrences from the medical events from a single case-by-case situation as medicine is practiced from forgetting the genesis but the lack of thing that is

going to -- you know, it's something that would have an impact on a large population in the immediate area.

So here we want, the FDA wants to see the reports because there may be a trend developing here that is going to affect an awful lot of patients using something. So if there is a protocol or there is a device malfunction or there is a problem with a radioactive drug, you need to get -- I would think that would be picked up more on the medical event side, rather than the abnormal occurrence side.

CHAIRMAN MALMUD: Dr. Thomadsen?

MEMBER THOMADSEN: Out of ignorance because I don't really follow them, what are some of the reactor events? What is a typical reactor event that is reported? And how many people die from them?

MS. McINTOSH: I have no idea. Do you have that? I don't have the --

MS. LANZISERA: I don't believe there were any for this year, but the top part of the language, the 100 rad, the major forces of bone marrow, that also would be typical to any of the reactor facilities. The 250 exchange, that would be 100 rad for the reactor facilities.

MS. FLANNERY: Dr. Malmud?

CHAIRMAN MALMUD: Yes?

MS. FLANNERY: There is somebody back here who probably could answer that specific question.

MS. BUSH-GODDARD: My name is Stephanie Bush-Goddard. I am the Chief of the Health Effects Branch of the Office of Research. We actually are the office that lead the AO criteria.

In the last five years, about 90 percent of the events in the abnormal occurrence report have been medical events. The last reactor events were actually there were fuel events, a possible criticality or something like that.

But in the last five years, we have had no more than about five reactor events. And each year we average about 11 to 13 medical events in the abnormal occurrence report.

CHAIRMAN MALMUD: Thank you for that clarification.

Dr. Vetter?

MEMBER VETTER: Yes. Could we go back again? What is the intention of notifying Congress and the general public about these events?

MS. McINTOSH: The intent is to make them aware of events that the AO reporting requirement is a law required of us to report to Congress events that NRC considers significant from the standpoint of

public health and safety.

MEMBER VETTER: So it's quite subjective?

MS. McINTOSH: There is some subjectivity to that, yes, what we consider significant. And that I think is probably more easily defined on the reactor side of the house -- correct me if I am wrong -- than it is on the medical side of things, than it is on the medical application of radioactive material.

CHAIRMAN MALMUD: Dr. Nag?

MEMBER NAG: I would like to ask a question here. In most of the other reactors and so forth, you are not expecting to give radiation to the public. And, therefore, you have a limit set that we selected more than somewhat to the Board and so forth.

Here your objective is to give some radiation to that person. But I do not see anything here where if you did not give that radiation, that is an abnormal effect.

I would have thought that severe underdosing would be an abnormal effect. That is, if the tumor went to get 110 ray and it never got anything, it didn't get anything, that would have been an abnormal event. But nothing is listed on the underdosing side.

MS. McINTOSH: The first criterion that

must be met is that the event must be a medical event. And then after it is a medical event, we look at how much the patient was given that was not expected to be given. So that does rule out the underdosing, but the underdosing we feel is addressed. And, in fact, it is still a medical event.

MEMBER NAG: It is a medical event, but it will not be an abnormal occurrence.

MS. McINTOSH: No.

MEMBER NAG: And if, for example, there was an LMA or whatever, you are penalizing. What I'm worried about is because you are penalizing someone for a possible mistake in the upper side, the physician will try to lower the dose so that they don't make any -- you know, if they make any mistake, it will be on the lower side and not on the upper side.

And that is something I have seen in hospitals that physicians know that if they make an error and they gave a little too much, they would have a side effect cause on the face, then they would be either sued or, you know, they would have a medical event.

So that was the intent to bite down on the dose. And if you bite down on the dose and the

repellents or the tumor did not get cured, you do not have any penalty for that. That's where I'm getting at.

CHAIRMAN MALMUD: I think that Dr. Welsh was next, and then you are next after that.

MEMBER WELSH: I would like to just go back to Dr. Vetter's question, which I think is the key question of this whole discussion here. What does Congress and what do we feel we really have to report?

It would seem to me that you would want to reserve this abnormal occurrence definition to something that is very severe, perhaps that causes death or is life-threatening.

If 90 percent of AOs are in the medical field -- and I doubt that many people die -- it seems like we are grossly over-represented here. And, therefore, we should be choosing the option that is most stringent or saying that when that results in death or is life-threatening. And I think that that would be the most practical solution to this dilemma that we're facing at the table here.

CHAIRMAN MALMUD: Excuse me. Are you saying that results in death or life-threatening in the opinion of a consultant physician?

MEMBER WELSH: If that is what is required

by NRC to have that consultant make that opinion, yes, that would be --

CHAIRMAN MALMUD: Are you suggesting, then, option 4 with one change? And that is that a phrase referring to "likely to generate high public interest" be dropped?

MEMBER WELSH: Correct.

CHAIRMAN MALMUD: That's option 4, part 1. Part 2, it says, "significant impact on patient health as determined by an NRC consultant physician."

MEMBER WELSH: Is that the NRC?

CHAIRMAN MALMUD: Well, by a consultant physician? By a consultant physician.

MEMBER FISHER: A regulatory consultant physician.

CHAIRMAN MALMUD: I beg your pardon?

MEMBER FISHER: A designated regulatory consultant physician. It's not just any consultant.

CHAIRMAN MALMUD: Well, then it's an NRC-designated consultant, NRC or agreement state-designated consultant physician, NRC or agreement state-designated consultant physician. Let's try that wording, if we may. And I think, having listened to this discussion, that that might meet the needs of most, if not all, of your concerns.

Dr. Nag?

MEMBER NAG: Just a slight modification from what you have stated.

CHAIRMAN MALMUD: Yes?

MEMBER NAG: I would say option 4, which is what you said, one.

CHAIRMAN MALMUD: Yes.

MEMBER NAG: And then it's option 3, 2.B. And that would be one other thing because otherwise a significant impact on patient health is not that clear, whether here the radiation exposure would result in permanent functional damage or significant health effects that would not have been expected. That's a little more clear, you know, I would say, number one, option for number 4 plus option 3, number 2.B. It would be really clear or more clear than what you have now.

CHAIRMAN MALMUD: Well, may I just question you about that? When you get informed consent from a patient prior to treating, is it not common to tell the patient that the risks include some of these terrible things, such as radiation to the bladder, impotence, et cetera, et cetera?

And, therefore, when you say "would not have been expected," they were in a sense expected

because they were part of the informed consent.

MEMBER NAG: Well, not really. I mean, the reality is the next day you may have bladder damage and so forth. That is more risk, but you don't really expect that from a regular treatment.

But that is where I think the medical objection was coming to be, that in the normal course of events, would this treatment have for us that damage?

You know, quite simply, the tumor is in the rectal- vaginal septum, between the rectum and the vagina. If you have damage to the rectum in that stage, that stage almost I wouldn't say is expected, but there is a high likelihood. And I don't think a physician would say that is unexpected.

If the tumor was somewhere else and it resulted in damage to the rectum, you would have upset that in your consent. You know, that is not something you expect to happen. And that would be an incident that is an unexpected event.

CHAIRMAN MALMUD: Well, then, if I may again, what about if we do a merger of these two, namely option 4, part 1, no change; part 2, a significant impact on patient health? That would result in permanent functional damage or a significant

adverse health effect as determined by --

MEMBER NAG: Yes.

CHAIRMAN MALMUD: -- the NRC consultant physician?

MEMBER NAG: Yes.

CHAIRMAN MALMUD: How's that?

MEMBER NAG: That's fine. I mean, that is similar to what I said.

CHAIRMAN MALMUD: Yes, yes.

MEMBER NAG: I fully agree with you.

CHAIRMAN MALMUD: I am just trying to think of both sides of it, namely protecting the patient, at the same time not putting the radiation oncologist at undue risk for having made an error that was one of the errors that might occur.

Dr. Suleiman?

MEMBER SULEIMAN: Clarification. If the NRC is reporting to Congress 11-12 AOs and one or 2 reactor ones every couple of years, how has that been received? Is it a problem?

MS. McINTOSH: It's not a problem. It's just they're getting information that they have a low interest in.

MEMBER SULEIMAN: I mean, we have hundreds of thousands of these things.

MS. McINTOSH: I mean, it's not a problem per se. There's just not really much benefit from reporting these, relatively speaking, low-significance medical events to Congress.

CHAIRMAN MALMUD: When they are reported to Congress, then it generates a question from the Commission to us about whether or not we should be tightening the rules because I received that question in a private session.

MS. McINTOSH: So that could be a danger that maybe it's creating an artificial concern.

CHAIRMAN MALMUD: If we report trivial -- nothing that injures any of us personally is trivial. And, therefore, nothing that injures any member of the public is trivial. But if it's a relatively small risk and reporting it to Congress elevates it to the position of something that it is not and, therefore, I think that given the wording that was suggested by -- who suggested number 4? -- Dr. Welsh and Dr. Nag, combining that, I think we may have achieved what you are aiming for.

Rob Lewis?

MR. LEWIS: I appreciate the Committee's work on this. I think that we have to take it back; in particular, the aspect of high public interest.

And I certainly understand the subjectivity related to that, but the NRC's need will probably be framed, at least partially, in terms of high public interest.

For example, if a reactor narrowly avoided a meltdown or fuel facility narrowly avoided a criticality event, just by luck, that certainly needs to be reported to Congress. And we have to find a parallel situation in the materials world that needs to be reported to Congress.

Nobody was exposed of any dose in those situations. And, in fact, that is the reality, is we are revising the AO criteria because of what happened at a field facility that narrowly avoided a criticality which was not reported to Congress until a year later.

CHAIRMAN MALMUD: Yes, but this is a very different world. This is a medical world in which we are discussing sequelae to patients that don't occur often statistically but do occur in the practice of medicine. To report these routinely to Congress is to elevate them to a level of concern that may not be appropriate with regard to making legislation.

MR. LEWIS: I absolutely agree with that and understand what you are saying, but I do think that there needs to be leeway for an issue that will

have a high public interest for NRC to tell Congress that we think this is an issue that may have high public interest.

It's not the 19 things we have been reporting, but it is something. And we've got to define what that something is.

CHAIRMAN MALMUD: Therefore, your feeling is that the phrase "public interest" should somehow remain there?

MR. LEWIS: Well, I am just trying to be realistic with the Committee about we can take this feedback, but I think that the group that is working on the issue at NRC is going to have to include that in part of their debate. I know the senior management of NRC is looking for that.

CHAIRMAN MALMUD: Thank you for informing us. We have a member of the public, and then I think we have -- oh, you've been waiting longer.

(Laughter.)

CHAIRMAN MALMUD: You've been waiting longer. Okay.

MEMBER GILLEY: I just want to make one clarification. I've done 10 to 12 medical event investigations as team leader. And in no circumstances when we have had an under-exposure has

the patient not been treated adequately.

Physicians have always gone back and altered their treatment to get the best possible medical care. I don't want anybody in this audience to leave thinking that that is not happening and we have allowed that as part of their corrective action when such events are occurring.

CHAIRMAN MALMUD: Thank you for putting that in the record.

We have a member of the public.

MS. FAIROBENT: Yes, Lynne Fairobent with AAPM.

Dr. Malmud, a couple of things. One, I am concerned a little bit about the language where are mandating NRC or agreement state-designated consultant physicians. If this wording were to go through, this would have to be a case in every instance.

Debbie, what is the compatibility on AOs?

MEMBER GILLEY: I think that's a compatibility B.

MS. FAIROBENT: That's what I was thinking. And, just to reiterate what Debbie said earlier, there are many agreement states that currently do not necessarily bring in a consulting physician for every AO that occurs within their

jurisdiction. And they may not have the funds to do so. They may not have the authority to do so in all cases. So I think that needs some consideration.

The other thing is having spent over 30 years in most of my career in the reactor end, I do think we are sending a wrong signal to Congress. If you take a look at the history of what has gone up in the AOs, medical dominates.

And, yet, I would have to take issue with they are not on parallel. And I'm not so sure there is a parallel definition that we can come up with for what is in the reactor or fuel cycle world that is reported to Congress.

I do think with the heightened security, the heightened interest in Congress right now on what is happening with medical uses and medical sources from increased controls. Continuing the practice of reporting or dominating the AO reports with medical events may pose unwanted scrutiny and unwanted legislation to come down the road that none of us is looking for.

So I just want to throw that balance out as for both the Committee as well as the staff to consider because it is not as simple as coming up with a one-to-one match in the materials, especially in the

medical material sides.

CHAIRMAN MALMUD: Thank you.

Dr. Thomadsen?

MEMBER THOMADSEN: In our proposal there, what would actually trigger a call to the NRC or to the agreement state? I don't see that it's at all clear what would be considered an incorrect administration, particularly if we assume that you can do all this dose incorrectly and it has no effect. What would be an incorrect administration?

CHAIRMAN MALMUD: Well, 100 millicuries of I-131 orally to a woman who is pregnant.

MEMBER THOMADSEN: Well, we are leaving out the fetal situation because we have already said that's not under this. That's under a different rule.

CHAIRMAN MALMUD: A hundred millicuries --

MEMBER THOMADSEN: Well, if you give 100 millicuries of iodine to somebody who is expecting a prostate implant, I think that would probably fall.

CHAIRMAN MALMUD: What about two patients scheduled the same day: One to receive 10 millicuries for hyperthyroidism, the other to receive 100 millicuries for thyroid cancer, and the doses are switched, they both have last names Johnson?

MEMBER THOMADSEN: Would you expect to

have any significant impact on the patients?

CHAIRMAN MALMUD: Yes. The 100 millicuries to a patient with an intact thyroid could result in -- well, definitely will result in wiping out the thyroid but could result in a release of hormone, which would also cause the patient some acute distress.

MEMBER THOMADSEN: In that case, you don't need anything before you get to the two there. I would say it is for medical licensees, any administration with significant impact. You don't have to even have any of that stuff.

MEMBER WELSH: Can I ask a question?

CHAIRMAN MALMUD: Good point.

Dr. Welsh?

MEMBER WELSH: Maybe I'm misunderstanding something, then. Do these have to be medical events?

MS. McINTOSH: Yes.

MEMBER WELSH: So that's what it is. It's a medical event that results in. So I think that answers.

MEMBER THOMADSEN: How do define a medical event, then? Are you still keeping the same criteria that you had before?

MS. McINTOSH: Yes, 35.3045, yes.

MEMBER THOMADSEN: Okay. I thought that was replacing all of that.

MS. McINTOSH: No, no, no.

MEMBER WELSH: So perhaps we should use the more precise terminology, then, "medical event," not "results," then. And then there won't be questions like this.

CHAIRMAN MALMUD: A medical event, not results in.

MEMBER NAG: Do we need death? Because significant impact on the health, I mean, that is already a significant impact. So we probably don't even need death because if you have death, it is a significant impact.

MEMBER THOMADSEN: Well, no because you could have a significant impact on a patient's health that does not qualify as a medical --

MEMBER NAG: Well, it is a medical event that results in death.

MEMBER THOMADSEN: That's why I am saying you need to have that. You need to have that medical event in there.

MEMBER NAG: I'm saying death.

MEMBER THOMADSEN: I'm not saying you don't put that in there.

MEMBER NAG: I'm saying death.

MEMBER THOMADSEN: Death is a medical event.

MEMBER NAG: Why do you need death there?

MEMBER THOMADSEN: I've said that before.

MEMBER SULEIMAN: That is unexpected. I mean, you've got to differentiate between the serious possible anticipated side effects for oncology patients.

But I have no trouble recording those numbers. I mean, you're defining it in such a way that these are really problematic. And I think if I'm reading these reports, that's the base for medical practice. I mean, you're seeing some very serious by definition abnormal occurrences. And why should you be afraid of reporting those numbers?

I think the numbers are very small if you're only reporting a dozen a year. I mean, do you want to say zero? I think that's an impossible expectation.

CHAIRMAN MALMUD: If I may, we don't want to show zero. We want to show that we are monitoring this. At the same time, we don't want to alert Congress to issues which don't require congressional oversight because they are routine problems dealt with

by other methodologies in the practice of medicine.

MEMBER VETTER: I'd like to move that we support what is on the board there, that particular option, option 4, as a --

CHAIRMAN MALMUD: Dr. Vetter recommends that the proposal read as follows, "A medical event that results in: 1) death, or 2) a significant impact on patient health that would result in permanent functional damage or a significant adverse health effect as determined by an NRC or agreement state-designated consultant physician."

PARTICIPANT: Second.

CHAIRMAN MALMUD: It has been moved and seconded. Is there any further discussion of that?

MS. TULL: On 2.B, there would actually not have been a second on the normal treatment regimen. Do you want that piece in there or no?

MEMBER NAG: Yes.

MS. TULL: I mean, put it there and --

CHAIRMAN MALMUD: That would not have been expected from the normal treatment regimen.

PARTICIPANT: Yes.

MEMBER LIETO: Mr. Chairman? This is Ralph Lieto.

That is what you had suggested originally.

CHAIRMAN MALMUD: Yes, that's what we had suggested originally. Okay. So that is the motion, which has been seconded, on the floor. Any further discussion of that motion? Dr. Welsh?

MEMBER WELSH: Just for Rob Lewis' comment about likely to generate high public interest, I understand and appreciate the concern. But if we would include it in 4, it probably should have been included in 1, 2, and 3 as well. So I would say that unless people feel strongly, I am comfortable with dropping it altogether.

CHAIRMAN MALMUD: Mr. Lieto?

MEMBER LIETO: I would like to just support what Dr. Welsh said because if you look at the abnormal occurrences reported, the trend that was reported in our Subcommittee report, you would see that there were these numbers that were consistently between 10 to 11 or 5 to 11 events over the last 4 years.

And, yet, there's been nothing apparently that's coming back regarding those over those past four years of events that have indicated interest by Congress with those types of events.

CHAIRMAN MALMUD: Any further discussion?

MEMBER NAG: One other.

CHAIRMAN MALMUD: Dr. Nag?

MEMBER NAG: I'm wondering whether we can simplify. Actually, I like what you have there, but I wonder whether we can simplify it by just eliminating death because that is redundant. And then if you have death, that is a significant adverse health effect.

CHAIRMAN MALMUD: I believe -- I didn't draft this, and this is not my crafting. This is a Committee crafting.

MEMBER NAG: Right.

CHAIRMAN MALMUD: We have to all take credit for it. I think the death stands out as a terrible outcome which should be highlighted as an issue of grave concern.

MEMBER NAG: Yes, right.

CHAIRMAN MALMUD: No pun intended. And, therefore, putting it first is appropriate in this situation, I would suggest.

Sally?

MEMBER SCHWARZ: I'm sorry. I was just stating in terms of the FDA, that death is always stated in adverse reactions.

MEMBER SULEIMAN: Or life-threatening.

MEMBER SCHWARZ: Or death first.

MEMBER SULEIMAN: What is proposed is what

is on that screen?

PARTICIPANT: Yes.

CHAIRMAN MALMUD: Option 4.

MEMBER SULEIMAN: With the corrections?

CHAIRMAN MALMUD: With those corrections, which really are an amalgam of several other recommendations that were made. That is the proposal. Let's call the vote. All in favor?

(Whereupon, there was a show of hands.)

CHAIRMAN MALMUD: Any opposed?

(No response.)

CHAIRMAN MALMUD: Any abstentions?

(Whereupon, there was a show of a hand.)

CHAIRMAN MALMUD: One abstentions. Otherwise, all in favor. Thank you.

2:45 plus 30. We can take a break. May we take a break before we move on to Dr. Welsh and emerging technology.

(Whereupon, the foregoing matter went off the record at 3:12 p.m. and went back on the record at 3:32 p.m.)

CHAIRMAN MALMUD: Thank you all. We will get started now. Dr. Welsh, we will do his presentation on radioiodine label, phospholipid ethers, cancer diagnosis and treatment.

DR. WELSH: Thank you, Dr. Malmud and I will be talking to you today about these radioiodine labeled PLEs or phospholipid ethers and diagnosis and treatment. This, I think, is one of the most exciting things that will be coming along in 2008. These phospholipid ethers can be radio-labeled and the investigators has chosen to use radioiodine and are looking at I-125, I-131, I-124 for imaging.

The basis for this is the selective retention of these phospholipid ether compounds in malignant tumor cells but not in hyperplasias, inflammation and other benign conditions. Thus far, the investigators have demonstrated selective tumor uptake in all human and rodent tumor models evaluated. It says 30 out of 30. I think they've checked out over 40 now and the concept of the universal oncologic tracer with a magic bullet, this is the closest I've ever seen us come to it.

It's not taken up into the brain through an intact blood brain barrier. So you can have brain tumor imaging. It does accumulate in tumors in the brain but not in normal brain tissue.

There's an insignificant renal elimination which means that it doesn't accumulate in the bladder and therefore you can visualize the prostate or

prostate bed. Initial human investigations have confirmed that what is seen in rodents seems to be happening in humans as well as far as the imaging goes.

So how does it work? Well, nobody knows. It's one of those kinds of things that in theory did not receive the grub (phonetic) development as far as I understand. The phenomenon is that phospholipid ethers accumulate in malignant cells but not normal cells. Phospholipid ethers integrated into the cell membrane are degraded by phospholipase. Phospholipase D may be the principal one in this particular case and normal cells metabolize these products and clear them from the cells.

Something goes wrong in malignant cell membrane metabolism such that these phospholipases do not degrade phospholipid ether compounds and there's low, there is no metabolism of the parent compound and these small molecules are retained in the cell membrane.

So here's a brief summary of some of the accumulation studies. All of these are tumor xenografts of various histologies and they do seem to accumulate and are retained in the tumor cells.

On the other hand down at the bottom,

there were a couple of benign tumors that did not accumulate the phospholipid ether compounds. So it seems to be selective in malignant cells. Somewhere along the process of malignant transformation in addition to what we learned in the textbooks about molecular changes and genetic alternations, also something is going on with perhaps phospholipase D so that malignant cells cannot metabolize phospholipid ethers properly.

A company has been formed and it's called Cellectar and they have chosen a specific phospholipid ether analog and they call it the CLR1404. They have tested hundreds of these phospholipid ethers and found that short chain ethers with maybe five to eight carbons are metabolized in normal cells but longer chain compounds, 12 to 15 or 18 carbons, are not easily metabolized. That's where this 1404 is found to be the one that is retained longest in the normal cells, can be labeled with iodine and some preliminary results have been published.

Here's an example of imaging and they used I-125 here. You'll see that on Day One it does seem to accumulate in the tumor, but the interesting thing is that over time moving from left to right you can see that it is washed out through the remainder of the

body and now is selectively accumulated and retained in this adrenal tumor model.

Here's another model. This is a glioma. Again, this compound doesn't normally cross the blood brain barrier, but it does accumulate in brain tumors. So here are some of the images and a fused image along with post-mortem histology slide showing that this compound does appear to selectively accumulate in the normal tissue in vivo.

Here's an interesting comparison between the I-124 -- It used to be called NM404. Now it's CLR1404. The company changed the name for some reason. FDG is accumulating at that lesion at the top called I which is an inflammatory lesion. It's not accumulating. The NM404 is not accumulating there. Similarly, there is less uptake in the heart. There is a lot of accumulation of the FDG in the bladder. But there is less accumulation of the FDG in the two tumors in the -- and that's to be compared and contrasted with the image of the 1404 right here.

Here's another example. This is an intestinal adenocarcinoma and FDG versus I-124, 1404. The heart is quite bright in the FDG. The kidneys are illuminated and the bladder has a lot of activity. This is not the case as much with the I-124 labeled

1404, plus you see a lot more of the tumor here and that was -- Incidentally, these are the exact same mice in these particular studies. The same mouse is being imaged with one technique and then a different technique. So it's an internal control.

There are just some more illustrations of how this agent appears to be accumulating selectively in the tumor area but not in the normal brain. Supposedly it doesn't cross the blood brain barrier and it doesn't accumulate in the normal brain tissues. And that's what these images appear to be confirming.

Here's an example of pancreatic cancer imaging, axial, coronal and sagittal. You can see that it does accumulate quite brightly in these particular areas, in that one particular area.

Prostate cancer, this is always a challenge for FDG PET, but so far it appears that this 1404 compound accumulates in prostate cancer cells as well as the other ones and the interesting thing about this is that it's accumulating in all these different cell lines. I showed you a pancreas adenocarcinoma, a glioma. Here's a prostate cancer. There's something very interesting about the biology of this particular compound, but it remains to be a fairly elucidative. But hopefully it can be exploited clinically.

Here's an example of animal on Day Zero treated with a dose of I-125 label 1404 and you can see the time course, Day Zero, Day Four, Day Nine, Day 41 and the comparison was made with the untreated sibling group died at age 21 days after the treatment after the tumor was implanted. So the sibling which was untreated lives 21 days. This animal was euthanized at 80 days and apparently in good health.

So to summarize, these phospholipid ethers are selectively taken up and retained by all xenograph and spontaneous tumor models examined to date. And it's quite impressive on that.

The tumors, the cancers, take up these compounds with the adenomas, hyperplasias, and inflammatory lesions apparently do not. The uptake is independent of location. So primary tumors take this up. Metastatic tumors take this up. Regional lymph nodes also do.

The imaging characteristics of I-124 label phospholipid ether compounds in animal models seem to compare favorably to what we might expect to get with FDG and it enables brain and prostate imaging with PET, something that we don't presently have routinely available in the clinic and it doesn't accumulate in the inflammatory lesions.

There have been a few studies done on humans, I think, about a half dozen patients so far that just demonstrated that you can see where the compound is going in human tumors as just like in the animal models. Formal clinical trials are pending and are expected to start this summer.

I just wanted to introduce the staff and the Committee to this new agent and maybe new set of agents that at this very early preclinical phase, at this very early phase, show great promise and potential and I thought would be of great interest.

CHAIRMAN MALMUD: Thank you. It was fascinating.

Dr. Nag.

DR. NAG: What do you foresee are the -- implications and radiation safety implications?

DR. WELSH: Well, one of the things that we talked about just today was the use of iodine-131 in thyroid cancer patients and how if we are going to release them from the hospital we have to be reasonably sure that they're not going to expose people to more than a certain amount per year or people with metastatic cancer unlike the average patient who gets thyroid cancer ablation. I would imagine that this treatment might be done more than

once or twice or three times a year and therefore the exposure to any member of the public might exceed what our limits are per year and therefore I wonder if this is going to have to be an inpatient treatment for many of these people.

CHAIRMAN MALMUD: Dr. Eggli.

DR. EGGLI: From a clinical medicine point of view, this is really fascinating. I think nothing beats the speed of FDG being able to image a patient 90 minutes after injection rather than days. But for the tumors that are poorly FDG avid and prostate was one of your examples certain other cell subtypes like lobular, breast and mucinous colon that are poorly FDG avid it probably has really great progress I would think. It really looks nice. One of the other comments though is the mice were fasted for the FDG studies making the FDG look worse than it would probably look in the clinical situation if the mice had been adequately fasted.

But I think this is -- To have other PET isotopes available that allow you to link to molecules that will light up the tumors that FDG doesn't work for is really fascinating and the potential of this is really fascinating from a clinical point of view, not just for therapy but specifically for diagnosis.

CHAIRMAN MALMUD: Dr. Nag.

DR. NAG: Have you or any identified any false positives? Have there been updates? You've shown that there were negatives in so many things and positive in a number. But have you seen any updates in any other?

DR. WELSH: No.

CHAIRMAN MALMUD: So far none. All right. Dr. Schwarz.

DR. SCHWARZ: I'm just curious what human tumors you're looking at with the IND trial?

DR. WELSH: I had suggested a couple and it was pancreas, glioma, prostate and lung.

DR. EGGLI: Again, I would encourage the investigators to look at tumors where FDG works poorly and add breast and colon to that. I mean, bronchoalveolar lung is one of the other cell types that are poorly FDG avid. But from a marketing point of view if you want to break into the marketplace do something FDG can't do which again the bronchoalveolar lung, the lobular breast, the mucinous colon and the prostate which you've shown very nicely. Those are areas where FDG -- where essentially you don't have to -- where there's no competition.

CHAIRMAN MALMUD: But you're speaking of

diagnosis.

DR. EGGLI: Yes.

CHAIRMAN MALMUD: And you're speaking of diagnosis and treatment.

DR. WELSH: I think the term they have for it is a theragnostic.

CHAIRMAN MALMUD: Yes. Which you could do with a combination of, let's say, I-123 label for diagnosis and then switch to I-131 or I-125 for therapy without having stunned the tumor assuming that it works. And so --

DR. SULEIMAN: Yes, I wanted to clarify. This Suleiman. Yes, the FDG is just used for monitoring and basically for possible therapeutic outcome. But this is a therapy and so I would hope that there's some effort at some accurate dosimetry --

(Laughter.)

-- which we've seen. I mean it's been problematic with the radiotherapeutic pharmaceuticals.

DR. NAG: Yes.

DR. SULEIMAN: And the other thing just to educate the two clinical endpoints really that the Agency will probably look for is what progression increase or overall survivability and so I would encourage they focus on trying to keep the studies

simple.

DR. FISHER: What's the uptake time?

DR. WELSH: Don't know the answer to that. In humans, I don't think that the answer is available.

DR. EGGLI: From the slides on mice, it was days.

DR. FISHER: Was it days?

DR. EGGLI: If you looked at the progression of the slides, it was days.

CHAIRMAN MALMUD: The ones that had the days labeled on it.

DR. FISHER: You need a longer --

CHAIRMAN MALMUD: -- number. Well, I-131 certainly has it and I-125 also.

DR. FISHER: But this mechanism suggests that -- entered like astatine-211 targeting the cell membrane might be ideal.

DR. EGGLI: I agree. You can get it targeted quicker.

DR. WELSH: I believe that the individuals at the company considered various isotopes and elected to go ahead with I-131 as their chosen radioisotope because they felt that it had least risk of non-efficacy in early trials and because it's easy for

them to manipulate.

CHAIRMAN MALMUD: Dr. Eggli.

DR. EGGLI: And again let me come back to what I do which is the diagnosis. I think in I-124 labeled radiopharmaceutical has huge potential benefit in the diagnostic arena. You know, you may subsequently follow with a therapeutic application with I-131 but there is huge potential in the diagnostic arena with an I-124 label.

DR. WELSH: And it would allow dosimetry beforehand as requested.

DR. EGGLI: Right.

DR. WELSH: And do quantitative pretreatment dosimetry response.

CHAIRMAN MALMUD: Any other questions for Dr. Welsh or comments?

DR. WELSH: One final point that I do recall being discussed with some of the investigators was in relevance to the difficulty of obtaining isotope. For a group of investigators who have started a company and hope that they'll have a success, there was some serious concern about the reactor in Ontario going down and the brief limitation that was placed on clinical and research activities and I think they are acutely aware of that and I don't

know what the solution is going to be.

DR. EGGLI: And the reactor only goes once every five years.

CHAIRMAN MALMUD: The I-131 is relatively ubiquitous in terms of its availability for medical use nationally.

DR. EGGLI: Until the reactor goes down in Canada.

DR. FISHER: With one supplier in Canada Ontario that one reactor goes down and you're out of I-131.

CHAIRMAN MALMUD: It hasn't happened yet.

DR. EGGLI: Well, the Canadian government shut it down a few months ago.

CHAIRMAN MALMUD: Dr. Schwarz.

DR. SCHWARZ: I'm curious as to --

(Telephone conference announcement.)

-- produced the I-124 -- in Wisconsin.

DR. WELSH: This is happening --

DR. SCHWARZ: The I-124 is being produced in Wisconsin. Who is producing the I-124?

DR. WELSH: These studies were done at the University of Michigan and are they done at Mass as well?

DR. SCHWARZ: And in Wisconsin. Correct?

DR. EGGLI: Yes, but almost any commercial radiopharmacy these days will cook up I-124 for you.

CHAIRMAN MALMUD: I-124, no.

DR. SCHWARZ: No, they won't. Just a positron.

DR. EGGLI: PETNET will make it for us.

DR. SCHWARZ: Well, there are certain ones that will but not everyone certainly. We've made I-124 at Wash U. but we don't routinely ship it. I mean, there are very selective places. So if you're close to one, that's good.

CHAIRMAN MALMUD: The interesting thing is that it doesn't really matter at this point because what you want them to do now, what they want to do now, is to identify as a diagnostic agent and --

(Telephone conference announcement.)

-- as a therapeutic agent -- either I-123 for diagnostic or with I-131 and even I-125. So there's a choice of isotopes of iodine other than the positron.

When we used to develop radiopharmaceuticals we always hoped we could label something with iodine because it was so readily available and technetium chemistry is such a dog. So you have to write up isotope and assuming that it

remains available to you. You have to be an optimist and assume that it will. It sounds very promising.

All right. So, if we may, we'll move onto the next topic.

(Whereupon, at 3:55 p.m., the proceedings adjourned to resume in Closed Session.)