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UNITED STATES OF AMERICA

NUCLEAR REGULATORY COMMISSION

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ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

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OPEN MEETING

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FRIDAY, SEPTEMBER 23, 2011

The meeting was convened in Room T2-B3 of Two White Flint North, 11545 Rockville Pike, Rockville, Maryland, at 8:00 a.m., Leon S. Malmud, M.D., ACMUI Chairman, presiding.

MEMBERS PRESENT:

LEON MALMUD, M.D., Chairman

BRUCE THOMADSEN, Ph.D, Vice Chair

MILTON GUIBERTEAU, M.D., Diagnostic Radiologist

SUSAN LANGHORST, Ph.D., Radiation Safety Officer

STEVEN MATTMULLER, Nuclear Pharmacist

CHRISTOPHER PALESTRO, M.D., Nuclear Medicine Physician

JOHN SUH, M.D., Radiation Oncologist

ORHAN SULEIMAN, M.D., FDA Representative

WILLIAM VAN DECKER, M.D., Nuclear Cardiologist

LAURA WEIL, Patients' Rights Advocate

MEMBERS PRESENT (CONT'D):

JAMES WELSH, M.D., Radiation Oncologist

PAT ZANZONICO, Ph.D., Nuclear Medicine Physicist

NRC STAFF PRESENT:

JAMES LUEHMAN, Acting Director, Division of Materials Safety and State Agreements

CHRIS EINBERG, Designated Federal Officer

ASHLEY COCKERHAM, Alternate Designated Federal Officer

MICHAEL FULLER, Alternate Designated Federal Officer

NEELAM BHALLA, FSME/DILR/RB-B

SUSAN CHIDAKEL, OGC/GCLR/RMR

SAID DAIBES, Ph.D., FSME/DMSSA/LISD/RMSB

KERSTUN DAY, OE/EB

JOSEPH E. DeCICCO, FSME/DMSSA/NMPD/SMP

JONATHAN EVANS, FSME/DILR/RB-B

SOPHIE HOLIDAY, FSME/DMSSA/LISD/RMSB

DONNA-BETH HOWE, Ph.D., FSME/DMSSA/LISD/RMSB

DEBORAH JACKSON, FSME/DILR

VARUGHESE KURIAN, FSME/DWMEP/DURLD

ED LOHR, FSME/DILR/RB-B

ANGELA McINTOSH, FSME/DMSSA/LISD/RMSB

KEVIN O'SULLIVAN, FSME/DILR/RB-B

NRC STAFF PRESENT CONT'D:

PATRICIA PELKE, R-III/DNMS/MLB

GRETCHEN RIVERA-CAPELLA, FSME/DMSSA/LISD/RMSB

DUANE WHITE, FSME/DMSSA/RMSB

SHIRLEY XU, FSME/DMSSA/LISD/LB

ALSO PRESENT:

ARMIN ANSARI, Ph.D., CDC

KAREN BISHOP, JOHNS HOPKINS HOSPITAL

ART CHANG, CDC

PETER CRANE

ANDREA CUZMANES, JOHNS HOPKINS HOSPITAL

WILLIAM DAVIDSON, UNIVERSITY OF PENNSYLVANIA

LYNN EVANS, Ph.D., CDC

LYNNE FAIROBENT, AAPM

MARC GARLAND, Ph.D, DOE

MICHAEL HAGAN, M.D. DEPARTMENT OF VETERANS' AFFAIRS

TRACI HOON, JOHNS HOPKINS HOSPITAL

FAIZ HUSSAIN, JOHNS HOPKINS HOSPITAL

ALBERT HYACINTH, CDC

FRANCES JENSEN, M.D. CMS/HHS

ROBERT JONES, Ph.D., CDC

IRA KREFTING, Ph.D., FDA

ALEX LIMA, JOHNS HOPKINS HOSPITAL

ALSO PRESENT CONT'D:

KATHY LISING, JOHNS HOPKINS HOSPITAL
MARY McCORMICK, Ph.D., JOHNS HOPKINS HOSPITAL
JANETTE MERILL, SNM
GEORGE MILLS, M.D., PAREXEL
THALIA MILLS, Ph.D., FDA
ADRIAN NUNN, Ph.D., BRACCO RESEARCH
MICHAEL PETERS, ACR
DENNIS PHILLIPS, DOE
SATISH PILLAI, Ph.D. CDC
MICHELLE PODGONIK, CDC
COURTNEY RADCLIFFE, JOHNS HOPKINS HOSPITAL
DWAINE RIEVES, Ph.D., FDA
GLORIA ROMANELLI, ACR
WOLFGANG RUNDE, Ph.D., DOE
DAVID SAUNDERS, CDC
JOSEPH SHONKA, Ph.D., CDC
LAURA SIERRA, ALSTON & BIRD
CINDY TOMLINSON, ASTRO
ANN WARBICK CERONE, MDS NORDION
ROBERT WHITCOMB, Ph.D., CDC
JENNA WILKES, ASNC
GARY E. WILLIAMS, VA NHPP
LUCIE YANG, Ph.D., FDA

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Adjourn

P R O C E E D I N G S

8:14 a.m.

CHAIR MALMUD: Good morning, everyone. And welcome to the second day of this session of the Advisory Committee on the Medical Uses of Isotopes. I'm Leon Malmud, the Chair of the Committee.

A few housekeeping issues first. Dr. Howe has kindly distributed to the members of the Committee this handout which will go under Tab 13. It's in the manual so that you have it right in front of you. It's been distributed. For those members of the audience who are with us, the public who are visiting with us, there are several more copies available if you care to obtain one.

We'll begin the session with the discussions regarding strontium/rubidium from both the FDA and NRC perspectives. The FDA perspective will be presented by Dr. Orhan Suleiman, a member of this Committee as well. The section on the NRC perspective will be presented by Dr. Donna-Beth Howe, also a member of the NRC staff who has been extraordinarily helpful to this Committee.

So if we may, we'll begin. I apologize for the delay. It was not due to any of the deficiencies of the members of the Committee. There was an audio-

visual issue which has been resolved. And with that, we'll ask Dr. Suleiman to start.

MEMBER SULEIMAN: That's okay. I can see it.

Good morning. I'll be presenting a brief overview regarding the recent recall of the Bracco CardioGen-82 rubidium generator. Since this is an on-going investigation, I will only present information that is either already in the public domain or Bracco has allowed us to share with you. If I happen to express some of my professional opinions during this talk, they are not necessarily official FDA or HHS policy.

I've also asked our medical officers at FDA who have been actively involved with this issue to accompany me today. Two of them aren't here yet. I think they must be hurtling through the security process. But Dr. Dwaine Rieves is the Director of the Division of Medical Imaging Products. This division is located within the Office of New Drugs in the Center for Drug Evaluation and Research. Dr. Lucie Yang, who is to my left, is the Team Leader who is responsible for the CardioGen-82 product. And Dr. Ira Krefting, who also hasn't arrived yet, is the Division's Deputy Director for Safety.

A brief technical review, I don't want to go into too much detail, but I think you need to at least get a grasp that this is a different type of generator. Rubidium-82 is a myocardial infusion agent with an effective dose in the 3 to 4 millisievert range. I'll discuss doses a little bit more later. It emits a positron which interacts with an electron and emits two annihilation photons of 511 keV, along with a 776 keV gamma, which helps distinguish it from other positron emitters used in PET imaging.

Although rubidium-82 is a positron-emitting nuclide, this is not your conventional PET nuclide which is often produced in the local cyclotron. Rubidium-82 is produced in a generator. Generators are not medical devices. They are considered part of the drug manufacturing process subject to GMP, or good manufacturing practices, and regulated by FDA and by the Center for Drug Evaluation and Research.

The parent nuclide for this generator is strontium-82 which decays with a 25-day half-life to its daughter product, rubidium-82, which actually has a 75-second half-life. They exist together in what's known as secular equilibrium. Strontium-82 is not

detected directly. It's detected by the rubidium's emissions. Also present with the strontium-82 is strontium-85, a product of the production process.

For medical use, the rubidium is separated from both strontiums by elution through a chemical column with a solution of saline. So essentially the strontium is above the column, and when you're ready to undergo the medical procedure the rubidium hopefully is extracted, eluded, and the strontium stays behind and eventually is injected into the patient.

Early in the year, two patients, which we refer to as the index patients, underwent CardioGen-82 cardiac imaging studies. One of these patients was scanned in Florida. The other patient was scanned in Nevada. They both left the country and when they re-entered the U.S. at different border entry points, they triggered radiation detectors and had spectral surveys performed. It was discovered that they had unexpected levels of strontium-82 and strontium-85. The spectral was analyzed by Los Alamos and FDA was eventually notified. The fact that they had undergone their scans several months earlier clearly raised everyone's concern. I think Homeland Security and Customs Border Protection really need to be

complimented. They were pretty vigilant, but I guess that's what they're supposed to do.

(Laughter.)

Los Alamos National Laboratory, in a publicly-available report, positively identified the unique photo peaks associated with those nuclides. Clearly, breakthrough limits have been exceeded. Breakthrough was independently verified by subsequent whole-body scanning initiated by Bracco at Oak Ridge National Laboratories for both of these two index patients. Bracco has committed to continue such counting during this entire investigation. And they've been very helpful.

This is the spectra reported in the Los Alamos report. The blue spectrum is associated with the strontium-82's daughter rubidium-82 and shows a unique 776 photo peak here, if you can see it to the right. That really distinguishes it from the annihilation photons. And the 511 keV annihilation photons which are over here for those who can't see clearly.

The longer the patient has been contaminated, the more the strontium-85:-82 ratio changes because remember the strontium-85 has a 67-day half-life. So it's lingering around much longer. The

strontium-82 only has a 25-day half-life. So depending on the ratio, you can get an idea of how long it was -- since the patient was actually injected. But that's been available from patient records anyway.

At this point, we basically wondered are there other patients out there and if so, how seriously were they contaminated? The next four slides review our July 15th FDA drug safety communication. And I have to admit I think it was written pretty well, where we expressed concern for the contamination of the potential for increased radiation exposure to patients.

When this presentation was prepared, we were not sure what numbers we could share with you, but we now have been given permission by different parties to share some of the information. So I will mention some numbers during this talk. The amount of breakthrough for the two index patients exceeded limits by 125 and 40 times for the strontium-82 and 7 times both for the strontium-85 component. Although this clearly suggested a problem with the generator regarding excessive breakthrough, why was it breaking through, a questionable safety testing for breakthrough at the sites was also in question.

We considered the risk at this time of

radiation harm to these two patients minimal, which was similar to the amount of radiation patients may receive from other radiation exams. But again, two patients detected at the border, was this more prevalent? Was this more widespread, if at all? And were some of the patients exposed to much higher amounts of contamination? So there was a public health concern that started to creep in. We had to look beyond our immediate regulatory authority of the medical product, the generator, why is not performing the way it was specified?

For initial radiation absorbed doses, based on the Customs' data, were estimated to be as high as 90 millisieverts or 9 rem. After whole body scanning at Oak Ridge, the estimated effective dose was 4.9 rem for one patient and 2.1 rem for the other. And according to the Bracco consultant, this was 10 times or 4 times greater than the expected 4.8 millisieverts.

Let me state here very carefully effective dose by itself is really inappropriate. It's a great metric for comparing doses from other procedures, but for medical risk assessment, for medical purposes, we really need to know the underlying organ doses. So I may be using effective dose here, but the real

critical issue is what are the doses that the different organs are receiving.

And just to emphasize the need for standardization, I just want to make a point here. If one were to use the actual Bracco product insert organ dose table which actually states that these patients should have received 1.2 millisieverts, rather than the 4.8 calculated by the Bracco representative, they would have received 38 times or 18 times greater than the product label.

There are several sets of organ tables out there: ICRP tables, the Bracco patient insert table, the current calculation which was using OLINDA software derived from Merck dose software, originally developed by the Society of Nuclear Medicine, Medical Internal Radiation Dose Committee. Using some of these other tables can yield higher or lower dose estimates. For consistency and standardization, we prefer to limit such dose estimates to one method, fully aware of these differences.

We considered the OLINDA methodology satisfactory. Did not want to become sidetracked over which organ dose table or method was more accurate. We felt that if there were serious levels of contamination, the dose differences would be much

greater than the differences or discrepancies among the different methodologies or organ dose tables. Having said that, as a member of this Committee, I believe, however, discussion on organ dose tables including the inherent level of uncertainty and how such dose estimates fit into the NRC's medical event criteria warrant a separate discussion, not necessarily for this session.

One major concern was identifying the root cause of the generator's failure, how widespread this was in terms of number of patients and what sort of radiation doses that some of these individuals actually received. Again, two patients are not an adequate sample. And there was an overriding tension in that the longer we waited to look at some other patients, the more the radioactivity would decay away.

There was much we didn't know then and we still don't know if this is a safety issue or a product problem involving generator failure, user error, or a combination of these. And there's some other factors that we haven't even brought to the table because the drug is administered with an injection system which is actually considered a medical device as well. And so there are questions in terms of the accuracy produced associated with that

product. Obviously, we've been discussing this with Bracco, the Nuclear Regulatory Commission, as well as several other state and federal agencies.

As we stated in our July 15th publication, we didn't know and as I said at this point we have a better idea, but until -- FDA is a science-based agency and we respect opinions, but we really prefer facts better. So we need more data.

After meeting with Bracco and discussing our concerns, including the results of on-going investigations, Bracco voluntarily recalled the CardioGen-82 generator until a lot of the safety issues were resolved. As I said, at this time we haven't really determined the root cause of the problem.

In summary, right now there are investigations going on with Bracco, the State of Florida, and the State of Nevada. Patients are being tested and whole body counting will be performed on a number of these patients. And in closing, I actually want to thank everyone involved. It's been a bit stressful for some of the stakeholders, but the State of Nevada actually moved very quickly and has been testing patients for the last several weeks and at this point has tested about 200 patients from Nevada.

And all I can say right now is there are a number of them that are contaminated, but until some better dose estimates are derived, I think it's probably -- wait just to see how all this plays out.

Also, I learned yesterday evening, that the State of Florida had actually begun testing some patients as of last Tuesday or Wednesday. And we can answer questions later.

CHAIR MALMUD: Thank you, Dr. Suleiman. Dr. Howe.

DR. HOWE: Orhan has given you a lot of the technical details. And what I'm going to talk about is the regulatory aspect of this. And I have passed out a handout of our regulations and how they fit into this and what we're looking at.

The first one is 35.204, the permissible moly-99, strontium-82, and strontium-85 concentrations. Our requirements and the requirements are the same as in the recommended state regulations that a licensee may not administer to humans a radiopharmaceutical that contains more than .02 kilobequerels of strontium-82 per megabequerel of rubidium-82 chloride injection or more than 2 kilobequerels of strontium-85 per megabequerel of rubidium-82 chloride injection. So that's our

requirement. You cannot -- you are not to give any more than that.

How are licensees supposed to know that they've reached this maximum permissible concentration? If they use a strontium rubidium generator for preparing the rubidium, they shall before first patient use of the day, measure the concentration of the radionuclide strontium-82 and strontium-85 to demonstrate compliance with the paragraph above. And licensees are also required when they do make this measurement to keep a record.

So our requirements, as well as the requirements in the states, are to measure the eluant for maximum permissible concentration before first patient use.

The records that they have to keep are in 35.2204, records of molybdenum-99, strontium-82, and strontium-85 concentrations. That says a licensee shall maintain a record of -- I'll skip the molybdenum part -- strontium-82, strontium-85 concentration tests required in the earlier requirement for three years and it has to include for each elusion the ratio of the measures expressed in kilobequerels of strontium-82 per megabequerel of rubidium-82 and kilobequerels of strontium-85 per megabequerel of rubidium-82 and

the time and date of measurement and the name of the individual who made the measurement. So we should have a clear record at licensee sites of these measurements and the ratios.

While we've been looking at these things we've discovered that some licensees may not have understood how to make the test. It's a very particular test. It's a lot more involved than the technetium generator breakthrough elusion test. And one has to be very precise with it, so there may be problems in following the manufacturer's instructions. There may be other issues with equipment associated with making the measurements also.

So the first level of regulatory interest is whether an individual has been given in excess of the permissible limits of strontium-82 and -85. The second level of interest is when that activity reaches a high enough point that a medical event needs to be reported. And the medical event reporting requirements are in Subpart M, 35.3045, report and notification of a medical event. And in that regulation, a licensee is to report any event except an event that results from patient intervention which we don't have here, in which the administration of byproduct material, radiation from byproduct results in a dose that

differs from the prescribed dose. In this case, if you were to get a normal rubidium procedure and you get two injections, one for resting and one for stress, and the maximum activity that the manufacturer recommends is 60 millicuries, and in our patients that have had whole body scanning, it's been more like a total 75 millicuries, then the maximum activity that you would expect would be .48 rem. So the dose, if it differs from the prescribed dose, it would have resulted from prescribed dosage by more than 5 rem. And we're getting close to that with one of the index patients. They're at 4.9 rem for the calculation. There's not precision in that calculation, but it is a good marker of the effective dose equivalent.

And then the other criteria, which is separate, would be 50 rem to an organ or tissue, or a shallow dose equivalent to the skin. And the total dose delivered differs from the prescribed dose by 20 percent or more. So right now, we're looking at differing from the prescribed dose by more than 20 percent. And then as soon as we hit the threshold of 5 rem effective dose equivalent or 50 rem to an organ or tissue, then we'll have a reportable medical event. At this point, we don't have a reportable medical event, but we could in the future.

And then if you do trigger a medical event, then the licensee has to notify the NRC no later than the next calendar day. What makes it interesting in this case is the licensees really don't have the ability to tell whether they will have a medical event or not until patients have been scanned. So they will probably be notified by the folks that are doing the scanning that there's an excess of 5 rem or 50 rem. And then the facility will have to make a medical event report.

And NRC has been actively involved in coordinating between FDA and the Agreement States. We've used our Memorandum of Understanding to be involved and follow what's happening. We have sent out an all-Agreement State letter after FDA did its drug safety notification, so that all the Agreement States were aware of what FDA's action was in the Bracco voluntary recall. And so we're actively monitoring and seeing at what point we need to get involved.

At this point, we don't have any identified patients at NRC licensees' facilities. That doesn't mean they're not there. They just haven't been identified.

CHAIR MALMUD: Thank you. So the investigation is on-going?

DR. HOWE: Yes, it is.

CHAIR MALMUD: And the purpose of presenting it to the ACMUI today is?

DR. HOWE: To make you aware of the public information that we can share with you and to let you know a feeling of the scope of what we know right now.

CHAIR MALMUD: Thank you. Are there any questions from members of the Committee?

Yes, Dr. Zanzonico.

MEMBER ZANZONICO: I have several questions. One is what's the -- you say the investigation is on-going. What are the components of the investigation? In other words, what information are you trying to solicit and where does that stand at the moment in terms of anticipating when and what if the product will again be available for clinical use?

MEMBER SULEIMAN: Let me answer it briefly, and then I'll defer it to the other people here. There's clearly the FDA medical product which is a generator. One very obvious question why did it fail in the first place? Without failure, the users wouldn't even need to do breakthrough testing. The second aspect is why was the breakthrough testing not done properly? That addresses, that's a user issue, a licensee issue.

You've got supposedly qualified personnel conducting this test. Are there deficiencies in how the test is done? So this is an area that's very, very nebulous, but it comes under very different regulatory authority. It doesn't -- FDA is really focused on product.

I think there's a bigger, broader public health issue. You've got patients out there that have used this medical drug and they may be contaminated. And you can argue whether the contamination is hazardous or not, but without knowing, how can you come to that conclusion? So I think there's that broader issue that's at play.

As I have introduced earlier, this is Dr. Ira Krefting. He's the Deputy Director for Safety. I introduced both of you in absentia.

DR. KREFTING: I was impressed with your Customs and Border Patrol. Yes, I'm Ira Krefting as Leon mentioned. And let me address that issue in further detail and add some granularity to the outline given by Orhan.

The investigation is multi-prong, multi-factorial in that obviously and most importantly the public health issue, identification of contaminated patients and quantification, as necessary, of the

underlying radiation that they received. So that is being carried on, as you heard, by some of the state agencies in concert with CDC and the NRC. Nevada has moved ahead very expeditiously screening or surveying a great number of patients. Florida is doing the same. CDC, in concert with -- there are plans for further screening.

The other aspect of that is we are concentrated on the product. We have what is called post-marketing requirements. This is part of our legislative mandate that was made in about 2007. The FDAAA Act, FDA Amendments Act, which requires us or allows us, if you wish, if we identify a new safety issue, to mandate that the sponsor do certain studies to help define and help us solve that particular safety issue to help -- so the sponsor is obligated to look into a safety problem. This constitutes a federal contract in that the sponsor is required to a study, present us with a protocol. There are milestone dates that the study gets done and then there's a final report, usually leading to some action on either the sponsor's part or our part, revision of a product, new labeling, etcetera.

In that regard, there are two post-marketing requirements which we initiated over the

summer. These are listed on clinicaltrials.gov. So the protocol, etcetera, is very public. One is to study patients in the two sites, two index sites that were mentioned in Orhan's presentation, Nevada and Sarasota, where patients who had received rubidium, undergoing clinical scans, at about the time as the index patients, the two identified patients had received theirs. So that's one post-marketing requirement.

Again, keeping with the theme, the concept that FDA primarily looks at the product, FDA has purview over Bracco, the manufacturer. The other PMR looks more broadly at the use of the product. The initial thoughts was that there may be breakthrough towards the end of expiry of the CardioGen generator. Basic chemistry sort of makes sense in that regard. The more elution that is put through the generator, the more saline to wash out the rubidium. There might be breakthrough towards the end of the life of that generator or when breakthrough was actually reported. So what's termed Study 105 is to look at patients who were receiving their rubidium scan, their rubidium CardioGen scan at the last date of use of the generator before it was sent back, before it reached expiry. So the hope there is that sites around the

country will participate in that study, will be able to survey patients looking back at the records that received rubidium on the date I just mentioned, the date of expiry.

I must emphasize to everybody that post-marketing requirement studies are voluntary studies. They constitute clinical trials. Patients come under all of the clinical trial protections that we're all so familiar with in the clinical environment. So everything I just mentioned is of a voluntary nature and the way the legislation and the regulations are set up, it is Bracco's responsibility to expeditiously execute these studies, move forward with them, help the sites in recruiting patients. And the first indications we have are that things are moving along in the regards that I just mentioned.

DR. YANG: To summarize what Dr. Suleiman and Dr. Krefting had said and to also directly answer your question, we're actually interested in what is a root cause; meaning is it a product failure or is it end user misuse or failure? That's one aspect of it. And the other aspect of it is what is the magnitude and extent of this increased radiation exposure, meaning how many patients out there in the United States have had increased radiation exposure as a

result of Cardio-Gen scans. And what is the highest radiation that any one of these patients may have resulted.

MEMBER ZANZONICO: This is Pat Zanzonico again. I guess my question is these patients were discovered fortuitously, at the borders. So can you summarize what data are available that are the basis for the regulatory limits? I guess my question is perhaps this isn't an abnormal occurrence. It's just something that was not detected previously because of less vigilance, just luck. And is it a possibility that this is the norm in terms of strontium breakthrough on this generator and that the regulatory limits may need to be adjusted to accommodate what now may be the actual behavior of this?

And I guess an ancillary question is has Bracco reported any change in manufacturing from its original formulation of the product to now that could be identified as a possible cause of increased breakthrough? Those are two separate, but related questions.

MEMBER SULEIMAN: I'll answer the first one. Let me tell you there's a lot of patients that are being -- that are scanned who don't have any breakthrough. A lot of the generators have been

tested. There are lots of examples of good practice. So this is not the norm.

A subpart of that though is we don't know if this has been going on longer. And again, when I say the problem, I'm talking about have people been using the product inappropriately? Have they not been performing the breakthrough testing properly? Or has there been an inherent problem, major, minor, with the column itself?

DR. YANG: I think that was a very good answer, number one. I'm not sure we can actually talk about number two. I think we will defer to our Division Director.

DR. RIEVES: My name is Dwaine Rieves, I'm Director of the Division. This product has been on the market for about 20 years. During that time, it's typical to have some changes in the product just because vendors go out of business, they get a new supplier, that sort of thing.

And so those iterations have occurred over the years. But in terms of the root cause investigation of the company, that is still ongoing. So far, the company has not identified a root cause in terms of the actual construct of the product itself.

There have, obviously, been iterative

changes over the years, necessary changes. But so far, I wish we had an answer, but it's going to be a few more weeks. The company is actively stressing these generators. These stress studies are ongoing. So hopefully within another six weeks or so, we'll have an answer.

MEMBER ZANZONICO: Can I ask a question?

CHAIR MALMUD: Dr. Zanzonico.

MEMBER ZANZONICO: Presumably, if the breakthrough were done at the point of service in the clinic where it was being used, these would have been identified. So your investigation now has disclosed that it's not being done or perhaps it was done, but not done properly? Or what's the status? That seems like a really key --

DR. KREFTING: All those points are very important. Those are all possibilities and those are all under active investigation.

MEMBER ZANZONICO: Okay, and one final point and I'll shut up. You know, some manufacturers certify users. Is that done in this case in terms of the QC? I mean it's not an overly onerous procedure, but it's not trivial either. Is that part of the marketing, so to speak, of the generator, kind of user certification by the manufacturers that they can, in

fact, use the QC properly?

DR. YANG: There is no certification process.

MEMBER SULEIMAN: By us.

DR. YANG: By us or by Bracco, the sponsor. But they do train the users when they actually first become customers.

MEMBER ZANZONICO: But there's no document provided that says User X has been trained and has demonstrated that he or she can perform --

MEMBER SULEIMAN: I'm not aware. We have representatives from Bracco here. If you want to comment on that, it would be nice. If you don't know any more than I do, then pass, you know. I mean for some products there is. I'm not familiar that this is actually required.

DR. NUNN: This is Adrian Nunn from Bracco. I'm not sure that we have complete records of who exactly has been trained and names, but we do train them and we know which sites have been trained. And we don't let them use the generator without that training first time around.

MEMBER ZANZONICO: Right, but does the company know of formal documentation?

DR. NUNN: Probably not of the sort that

you are looking for.

CHAIR MALMUD: Malmud. One of the items that you alluded to was that the problem may be attributable to the age of the generator and the amount of saline washed through in terms of the eluant so that toward the latter end of the use of a generator, there may be this problem which does not exist earlier in the use of the generator. Therefore, a question I have is was that tested for when the product was initially placed on the market?

MEMBER SULEIMAN: We've raised that question ourselves. The product was approved 22 years ago. I think Bracco didn't -- Bracco bought it from a previous company as well. We don't really know the answer.

CHAIR MALMUD: So we don't know the answer to that question.

MEMBER SULEIMAN: That testing actually is -- Bracco is repeating a lot of that as we speak.

CHAIR MALMUD: So that testing is ongoing currently.

MEMBER SULEIMAN: So we'll get some answers for that.

CHAIR MALMUD: Thank you.

MEMBER LANGHORST: I had a question, but if

you're not done --

CHAIR MALMUD: Dr. Langhorst, absolutely.

MEMBER LANGHORST: Thank you. Dr. Howe, in regard to our Agreement States that these two patients were treated, are there reports yet on their inspection with regard to 35.204 and 35.2204 as far as the site users performing the test and documenting the test?

DR. HOWE: Nevada has done an inspection of the facility with the patient that came across the border and tested positive. But that report has not been finalized yet.

MEMBER LANGHORST: Okay.

DR. HOWE: And the State of Florida has done an inspection of the site in Florida and has inspected a few other sites as well. And the results of that inspection are not available yet.

MEMBER LANGHORST: Okay, okay, thank you.

DR. HOWE: And I think it might be important to note the scope of the rubidium use when the generators were still in the market. And places seem to average somewhere between 4 to 20 patients a day. And they were running five to seven days a week, so there are a lot of patients that were out there, nowhere near the number you have for molybdenum, but a

really large number of patients.

CHAIR MALMUD: Thank you. Other questions? Yes. Laura, I think you were next, Laura.

MEMBER WEIL: This is Laura Weil. What kind of notification has gone out to patients who were imaged in these generators, using these generators, other than the clinical trial that's listed publicly which is recruiting?

DR. KREFTING: We, as was mentioned previously, don't have direct control over those type of communications and that type of communication is in the hands of the sites of the end users that actually do the studies. We understand around the country that some sites have notified patients about the situation. And we also understand that some sites have not.

DR. YANG: Adding on to what Dr. Krefting is saying, the sponsor's website, CardioGen, actually has like a link for patients and so --

MEMBER SULEIMAN: Also, our July 15th public communication pretty much was announcing it to the public, but it needed a little bit of stimulus.

CHAIR MALMUD: Excuse me, ladies and gentlemen, may I remind you that this is being recorded. And therefore would you please reintroduce yourselves each time you speak so that the court

reporter can record it accurately. Please go on.

DR. KREFTING: So in summary, it is the responsibility of the local sites to notify their patients if they felt so inclined. If they were to participate in the PMR studies I mentioned to you, that would be the responsibility of the local sites to invite patients to participate and during the state investigations, we understand that the sites themselves were notifying the patients and inviting them to come in for these state screenings.

The other two mechanisms were just as mentioned, there is the CardioGen website that has some patient general information on it, as well as our drug safety communication. Unfortunately, I can't give you a more detailed answer than that.

MEMBER WEIL: Thank you.

DR. KREFTING: I did want to speak to your question that you addressed to Orhan a few moments ago. Again, this is Ira Krefting. You asked about the elution information and how there was testing of the generators, perhaps at their time of approval back about 1989-ish. As Orhan told you, we don't have immediate information for you, the extent of testing at that time. But the more tantalizing information is that when you look at the use of the CardioGen

generator over the last few years, there has been an astronomical increase in the number of patients who are receiving the study.

It's perhaps appropriate because in the practice community, molybdenum is less of a radiation dose, as you heard. Some people feel the images are a little easier to interpret and a little better defined. So there's been this vast increase in the number of patients, probably well beyond the thoughts back in 1989 to the extent it was going to be used when it was first introduced in the market.

The other important point that was brought out by Dr. Howe and Orhan mentioned to you there is a vast difference in the number of patients who around the country at sites getting this. Some sites will do a couple patients a day. Other sites, like the most active ones can do 18, 20 patients a day and run the generator 7, almost 7 days a week. So obviously, the elution volume over that vast spectrum of patient input is going to vary tremendously.

CHAIR MALMUD: Thank you. Do we know the volume of patients handled in the two institutions sited in Florida and in Nevada?

DR. KREFTING: Yes, sir.

CHAIR MALMUD: Is it at the higher end?

DR. KREFTING: Yes. Nevada is probably the highest site in the country and the Sarasota site is in the top tier, probably top ten. I think it's probably top five-ish.

CHAIR MALMUD: Thank you. If I may, Dr. Howe, you mentioned that from the data thus far collected it did not appear that the limits set by the NRC have been exceeded in these patients. What is the target organ of the two elements involved, the strontium and the rubidium and how close to the limit have we gone from the data thus far collected?

DR. HOWE: The strontium is the bone surface. So you have the bone surface and the red marrow.

MEMBER SULEIMAN: One of the patients had doses -- what's the limit, 50?

DR. HOWE: Fifty.

MEMBER SULEIMAN: It's getting close to that, but didn't. And so none of the NRC's radiation dose medical event criteria have been exceeded.

CHAIR MALMUD: The purpose of my asking that question was that someone else asked if the patients had been notified and in fact, the limits have not been exceeded. Is that correct?

DR. HOWE: The limits haven't been

exceeded, but the patients that are being tested for radiation have been notified that there were issues with the generator and asked if they could come in and voluntarily participate and have a radiation measurement made. And so those patients are aware that there are issues with the generator and have voluntarily come in to have radiation measurements made.

We have not had the activation of the medical event reporting requirements yet.

CHAIR MALMUD: Again, the reason that I asked the question was that we've always walked a very narrow line between alerting patients to possible risks and panicking patients for risks that actually did not occur. So at the moment, recognizing the data is still being collected, we have not exceeded the limits that have been established by the NRC. Is that a fair statement?

MEMBER SULEIMAN: Officially, no. They haven't been exceeded. However, based on some of the preliminary data that we've seen, there may very well be some.

CHAIR MALMUD: At that point, we would expect that the patients would be notified of that area of concern rather than the current notification

of patients which is that we need to retest you with regard to a concern. A concern is not the same as an actual hazard. And I think that's what Laura Weil was addressing in her role of concern for the patient. So I wanted to make sure that we all understood that we were still in a gray area where we recognize that there is a problem. But it has not reached the level at which the patient should be notified that he or she may be at any kind of risk for having received radiation exposure in excess of that which is tolerable by NRC requirements.

DR. HOWE: And Dr. Malmud, you hit an important part. We have -- there are on-going radiation measurements made of specific patients in Nevada and in Florida because we have high reason to believe that there are excessive contamination in those patient populations based on the Homeland Security triggering.

CHAIR MALMUD: And also verified at Oak Ridge. Those measurements, there has been significant product breakthrough and these patients are contaminated without little doubt about that.

DR. HOWE: Yes. But what I'm saying is that we have not gone out to all the other facilities because you don't want to call patients back in and

unduly make them worry if, in fact, there weren't issues at that particular site. And we have seen, as Orhan has indicated, the data indicates that there are people that had procedures with no contamination. But there are others that have had contamination. So that's the issue we're balancing right now is when do you go to a site that hasn't been identified with a Homeland Security patient and start to call people in. And that's what FDA is talking about with the Bracco study and other studies.

CHAIR MALMUD: Another question if I may, and that is, currently are these generators being produced by any manufacturer, and (b) currently used in the United States for the record?

DR. HOWE: No, they are in voluntary recall.

CHAIR MALMUD: Total recall?

DR. HOWE: Yes.

CHAIR MALMUD: Thank you. The other issue is, of course, that --

DR. HOWE: And I believe they've also been recalled internationally.

CHAIR MALMUD: Thank you. I just want that in the record. Other questions? Oh, excuse me.

MEMBER GUIBERTEAU: Mickey Guiberteau.

Also for the record, since 1989 is this the first incident that has been discovered of nearly or significant breakthrough in terms of these strontium and rubidium columns?

DR. HOWE: NRC can't answer because we did not regulate them until the NARM rule came into effect which would be 2005-2007 time frame.

MEMBER GUIBERTEAU: But it is since that time, is that correct?

DR. HOWE: Yes, that NRC is aware of.

DR. KREFTING: Ira Krefting here. To further answer your question, breakthrough has occurred in the past. And that has, for example, looking back at the record, there has been a breakthrough in previous -- I believe it was 2010-ish or so, but those were reported to Bracco and appropriate actions were taken such as recall of that specific generator.

MEMBER GUIBERTEAU: And what did they find at that time?

DR. KREFTING: I don't know about the investigation at that time. I can't tell you.

MEMBER GUIBERTEAU: Could Bracco tell us, a representative?

DR. NUNN: Adrian Nunn. I'm not aware of

the details, but that concern was investigated and I think it has been concluded.

MEMBER GUIBERTEAU: And what was the outcome?

DR. NUNN: I don't know.

MEMBER GUIBERTEAU: Thank you.

CHAIR MALMUD: There was another question.

MEMBER PALESTRO: Chris Palestro. Many years ago, many, many years ago, strontium-85 was used for studying the skeletal system. I don't think it was imaging, it was scanning or counting of one sort of another.

So my question is do you have a sense of comparison between the doses that the index patients or however many patients you have a chance to evaluate who have been exposed to strontium-85, the doses that they've received in comparison to the doses of strontium-85 that were administered for diagnostic purposes many years ago?

MEMBER SULEIMAN: I am not aware.

CHAIR MALMUD: If I may, the studies that were done with strontium-85 were approximately 1965. The authors were Sklaroff, Charkes, and Young, a nuclear physician, a radiation oncologist, and a pathologist. The dosimetry was calculated. It's in

the literature. The articles, the seminal articles were published in the Journal of the American Medical Association which made the technique clinically available.

Initially, their work was done on a Pickerer scanner with paper, rather than film. They converted to film so there were images. The patient population at that time was composed solely of women who had metastatic breast cancer, proven by x-ray and therefore had a limited life expectancy by definition of the disease and the extent of metastases.

Therefore, the radiation burden was accepted in 1965 considering the limitations of the population.

When the technique became attractive, as a means of identifying bone metastases in excess of those that could be identified by whole body x-ray studies, the next substitution for -85 was strontium-87m which was a generator. The strontium-87m was a methodology used and there's dosimetry for it as well. It's documented in the literature. I'm not certain that I can give you the reference, but it was one of the IAEA or NRC publications.

Subsequently, because of the radiation burden of strontium-85 which was excessive by current

standards and then as well, and the impracticality of the -87m, a substitute was sought and that substitute evolved into a phosphate compound, an analog of calcium, but a phosphate compound, initially marketed as polyphosphate by a number of radiopharmaceutical companies. And that product evolved to the current products which are also phosphates, labeled with technetium-99m and therefore those technetium-99m products have been the products and remain the products which are used broadly for not only the detection of metastatic disease, but for inflammatory disease of the bone, trauma, shin splints, many things that are not well defined by radiopathy.

And that's how we got to where we are now. So the radiation burdens today are trivial compared to those of -85. And the data is in IAEA and in NRC publications from many years ago, as well as medical literature dating back to the middle 1960s.

DR. HOWE: Thank you, Dr. Malmud.

MEMBER SULEIMAN: Thank you, yes. And from '63 to '72, if my memory is right, the Atomic Energy Commission regulated the radio-labeled drugs. It wasn't until '72 that that authority was given back to FDA.

CHAIR MALMUD: That may be, but it was the

AEC at that time, not the NRC. You're correct.

MEMBER SULEIMAN: But it was also regulated. FDA did not, I think at that time the AEC regulated all radioactive products including drugs.

DR. HOWE: And I believe at that time the major group that was looking at the drugs for approval was the ACMUI. And it's Subcommittee on Human Use.

CHAIR MALMUD: Thank you. A little bit of history.

Dr. Zanzonico?

MEMBER ZANZONICO: Can I just make a comment, not a question? When my clinical colleagues learned that I was attending an NRC meeting where this would be on the agenda, I got some -- let me put it strident feedback to the effect that this is -- and this is not my opinion, this is what my clinical colleagues have told me, that this is a regulatory overreaction, that the negative impact on patients for the lack of availability of the generator does not justify the total recall.

And so at the very least, I would ask on their behalf that whatever regulatory and corrective action is required, that really be expedited because it's felt that it's gone on much, much too long to the -- in terms of negative impact, clinical impact on

patients. So that's just a little bit of editorializing that I promised I would bring before the meeting.

DR. KREFTING: Ira Krefting here. I appreciate that statement. I think it's important that that be answered and discussed here, if nothing else, for the public record and in understanding of the function of the FDA and to further review and reiterate the statements that have been made by my colleagues over the last few moments.

I also do some clinical practice on the side, so to speak, and you hear similar comments around, but I think it's important that we emphasize a couple of points. One is as we all alluded to a little bit earlier, rubidium, if the tests really work as stated and the radiation dose would be less to patients and that might be a good reason for consideration of this as an alternative of cardiac scanning procedure, but if it's not working as it should, if there's contamination of patients, without going into details, the dosing that these individuals are receiving is tantamount to approximately what they'd be getting with some of the more well known or tests that were available previously. But the more important point, as brought out by our drug safety

communications, is that we are concerned that even if the drug is used as directed, even if you follow all of the labeled recommendations, the handbook from Bracco, everything else, if you follow all that, there still may be the potential for breakthrough. And that's how we stated it in our drug safety communication, particularly the one, the latter one in July.

So I've been approached around the country by very good, well meaning physicians saying I do everything right, what's the problem? Well, the problem may be beyond you. It may be in that either as we're learning now as brought out by the other questions that maybe the labeling instructions are not adequate, even though they appeared adequate back in the '80s and '90s. Or maybe as you heard from my director, there may be some subtle changes in the manufacturing.

There may be something that when these devices are used with the high-patient throughput that was never anticipated back in that generation, with the high-patient input, maybe they are breaking down. Maybe there are structural defects that we need to elucidate because so many patients are receiving it. So I think it was important to respond to your

statement, sir.

CHAIR MALMUD: Thank you. Dr. Zanzonico's concern is a concern that the entire Committee has, namely, again we walk a narrow line between protecting the public, the patient from excessive radiation and denying the opportunity to a procedure that actually for a large number of people reduced the radiation. However, we are obligated under regulations to go through the process that we are and we hope that it will be as expeditious as possible which is what I think Dr. Zanzonico is request of us on behalf of those who spoke to him and those who speak to me about the same kind of issue.

MR. LUEHMAN: Dr. Malmud?

CHAIR MALMUD: Yes, Mr. Luehman?

MR. LUEHMAN: Yes, I guess one comment I would make in response to those people who have provided input to Dr. Zanzonico which is that if contacted by -- I think to bring -- to help bring this investigation to closure, then if in the studies that are going to be ongoing for patients who are yet unaffected or identified clinics, for those practitioners to encourage their patients to participate so that the FDA can get the broadest and clearest picture of the extent of this problem.

Because obviously, the more data we have, and if it all shows to be that the patients are receiving less than the amounts that you would expect with breakthrough, that's going to lead us to one direction and obviously focus in more on local practices at those institutions, or as was stated earlier, the idea that maybe the problem lies in the throughput.

So I guess I would go back to your colleagues and say well, if contacted by the FDA for a Bracco study that one of the best ways to get this behind us so to speak is to encourage participation on the part of patients, because I think that that's going to give us, give the FDA and the NRC the most data and allow us to draw the best conclusions in the quickest amount of time.

CHAIR MALMUD: Thank you. Other items? Yes, Steve Mattmuller?

MEMBER MATTMULLER: Hi, Steve Mattmuller. A couple of comments and a question. One in regards to the training by Bracco and maybe I need to disclose that we are a clinical site that has used the rubidium generator. And we're missing ours now and do miss it.

But the training by Bracco from my perspective, and I wasn't heavily involved in it, but was very extensive and the technical service people at

Bracco were well trained and very helpful. And it just wasn't they were in and they were out. It's been ongoing. In fact, not necessarily on generator issues, but they were also very helpful on scanning issues which we've been participating in some other issues or scanning protocols with them.

So I know we've had constant contact with the technical service people of Bracco on a number of issues, not directly related to problems, but our interactions have already been very positive and very good. But also to answer that question, do we have a piece of paper signed and documented? I doubt it. But I do know the training did take place and was very thorough.

The other statement and I'm sorry, I can't remember which FDA official mentioned it, there has been a dramatic increase in use of the product and part of that I would venture to say is one that's a very, and it may not be -- I would say the gold standard, the myocardial profusion imaging right now in the United States, for a number of reasons. Because it is a PET agent because of the higher energy and which also has definite advantages in larger patients.

And the other drug factor behind that is

the past headaches and lack of availability of moly-99 for technetium generators that I know some sites have moved to rubidium because they couldn't get technetium on a regular basis. But then once they found out how good the rubidium is, they've stayed with it.

And then just my final question would be for Orhan. You mentioned that preliminary data has shown that there are patients who were scanned at these index sites -- that's my question. Preliminary data has shown that some of these patients have exceeded limits, or you think they're going to exceed limits? Are they from index sites or are those from other sites?

MEMBER SULEIMAN: The first round of data is from index sites because we had a lot of difficulty getting a lot of things moving. So I think if we could have had all our questions answered one or two months ago, this thing could be much closer to closure. So the lack of data, the lack of information, couldn't move quickly. And we're going to be data driven. But the first tier was basically to focus on the index sites because that was a high probability. You can't go to non-index sites when you haven't even done the index sites.

The first focus, if we're going to bother

these patients, let's get them close to the index patients because it sounds like intuitively maybe at the end of the lifetime, the generator is breaking through more. We do plan on looking at patients earlier in that site. It's kind of terrible to have to use patients to determine the performance of a generator, but that's what we've been forced to do. And there are plans to look at some sites where nothing seems to be wrong.

I think at some point we'll have enough of a picture where we'll say enough, it's okay. I'd be more than happy -- I'd be more happy than anybody else if nobody was contaminated and all the doses were very, very low. And if you guys feel that that's comfortable, that's fine. But based on what we've seen, based on the fact that Customs had to pick up these first two patients and based on we have no history of how widespread and what sort of doses some of these individuals could receive, it's sort of a tiered stratified approach.

Ideally, you'd like to snap your finger and you deploy and you test these patients and everything is -- and then you've got the issue, hey, we've measured activity with different survey meters. And you get some sort of idea what the relative amount

of activity is, but how does that translate into actual dose?

So I was very pleased that Bracco offered and is committed to counting the patients with whole body scanning and much more definitive dose estimates. We agree, but opinions don't carry as much weight as data does.

CHAIR MALMUD: Other comments or questions, members of the Committee?

Dr. Van Decker?

MEMBER VAN DECKER: Thank you, Dr. Malmud. I guess a variety of comments and then I do have a question at the end.

You know, first of all, I want to personally thank both the FDA and the NRC for the preliminary briefing. I mean the provider community obviously gets bits and pieces and I was trying to figure out where we are and where we go and how we provide care to patients. And so preliminary data is always helpful to us to start discussion and we appreciate that.

I think I can speak a little bit on behalf of all my colleagues in the nuclear cardiology community and especially on behalf of ASNC. Our goal here is twofold. Number one, to create access for

patients for studies that have become a seamless part of cardiovascular care for people who have coronary artery disease which is still the number one killer, right, among every one in the United States. One person a minute dies of heart disease. So we're trying to make inroads on that.

As expressed to this Committee before, we've actually made some major inroads over the last 30 years and some of it has been due to the technology and that's been a good thing that you guys have helped facilitate our ability to deliver that care.

The second part of this equation which I think you guys are bringing up is we want to do it in the safest manner possible. I mean we want to make sure that we're within realms and that the I's are dotted and the T's are crossed and we can get this across a broad provider community and see how things play out. So the safety piece to us is important.

I point out to my colleagues on the Committee that I think over the last ten years we've learned a lot about the challenges in mechanical systems involved with delivering radiation that's useful, Gamma Knives, microspheres, vascular brachytherapy and some of the questions that come up along the way that we need to think through and make

sure that we're trying to do the best we can with that interaction which is never perfect.

I think to some degree this becomes a little bit of a test discussion for the understanding of generators themselves, parent-daughter relationships and other isotopes that may come to market, the whole general medical, nuclear medicine community may want to be utilizing.

So some concept of -- in the pill portion it's called therapeutic window, but in this portion, there's some window of safety for any device. What's the stressor to get you over that window? Are you so close to the stressor that it doesn't take much to get you over it? I mean what do we need to know about flow rates and total eluates over the month and end of week generators and that type of stuff.

And so the knowledge base, we think is very, very important and I think everyone wants to cooperate in getting that accomplished and whatever we can do to help in that regard.

I would say, I would offer at the table that ASNC certainly is very, very interested in being an educational piece of this to our membership and getting out whatever information needs to get out and is already working very hard on educational programs

on QC, once again in both SPECT and PET worlds for molytech generators to make sure that the community, irrespective of any tech papers that come out of this, gets distributed to people in the trenches that are trying to deliver care to patients. And I think you have or will have contact with -- I think you'll there's been quite a bit of activity done in that regard already.

We want to make sure that we've fulfilled documentation requirements and that's across the board, making sure that they make scientific sense here and where we're going. And so I would offer that the provider community clearly wants to be a piece of this and wants to move this along so that we can get things going on the right track again.

I guess my last question to all of this because I found this interesting, was I think that ASNC made an attempt to touch bases with FDA to see what it could do on a provider bases across the Society and was actually asked to write a letter with questions that would facilitate the discussion to get in the door which was done. But, you know, whatever can facilitate that process I think you'll find professional societies as a whole, across all the constituents that represent some of the greater

medical societies here are interested in being proactive in helping their membership and doing the right thing. And whatever we can do to be part of that process as opposed to being on the other side of a line, we're all taking care of the same patient, we all want to do the same thing, would be helpful.

That ends my little discussion. Thank you.

DR. KREFTING: Ira Krefting. Again, it's important to respond to those statements you've made. They're very positive statements in terms of what you can do as a provider, somebody taking care of patients and dealing with these sites as was brought up by one of the other gentleman. Encourage the site and the patients to participate in the PMRs, as I indicated in my initial presentation. Those are voluntary, voluntary on the site level. It's voluntary on the patient level, obviously.

In terms of FDA's outreaching working together we, this past week, had Dr. Andrew Einstein speak in what we call Visiting Professor Lecture Series exactly on some of items you just mentioned. Additionally, we've heard -- we got your letter.

We're in the process of setting up a meeting. We do this with -- this is not unique for your organization. We do this with a lot of

organizations as the need is necessary. It's educational. It creates an interaction and it provides us with feedback. I think we've also got to say as you hear in this discussion that this is a pending investigation. There are a lot of confidential issues here. There are a lot of regulatory possible infractions. So we can't talk about specifics. But we're set to meet with you guys.

MEMBER VAN DECKER: My point wasn't the specifics per se which is an issue that needs to be sorted out, but the question is we need to move forward and so we can be moving forward simultaneously with everything else, just based on some global concepts here. And everyone, I think, is happy to do that.

CHAIR MALMUD: This is Malmud. And so in summary, Dr. Van Decker, you're speaking on behalf of nuclear cardiologists and your eagerness to assist the FDA and the NRC with their investigation. And the FDA and the NRC are responding with enthusiasm to your offer.

(Laughter.)

CHAIR MALMUD: Is that a fair summary?

MEMBER VAN DECKER: Yes.

CHAIR MALMUD: Thank you. Are there other

questions? Yes, Dr. Welsh.

MEMBER WELSH: Jim Welsh. I know that this has been discussed already and the thought has not escaped anybody in this room, but I thought I'd just state it clearly for the record. I understand that there's an ongoing root cause analysis and we still don't know for certain whether there was any defect in the generator or if the problem is with the licensees, but using the Gamma Knife as an example, we know that this particular device, this generator might not be as complex as a Gamma Knife, but it's not trivial either.

And therefore, our role as an advisory committee is to provide some concrete advice. And again, using that Gamma Knife analogy, nobody is allowed to operate the Gamma Knife without having the vendor-specific training and a certification that says specifically this named individual has been trained by the vendor and anybody else who gets training and is authorized to use a Gamma Knife has to have some piece of paper that says he or she has received some training either from a vendor or from a qualified authorized individual.

So going forward, it would seem very appropriate that the manufacturers and/or users, who

are currently qualified to operate these generators, keep detailed records and name names for those who receive the training and who are qualified at the sites. It would be relatively simple, I would think, for the vendors to just say on this particular day we went to this site and provided the training and the following people were in attendance.

Similarly, I think it would be relatively simple for an institution to say that the following named individuals received the vendor training and have subsequently trained the following named individuals so that for patient safety, Joe Blow, who has never received the vendor training or received formal training from the qualified technician, can't on a day when the qualified technician isn't there, step in and think that he or she can perform the measurements adequately and find out that he or she is not qualified and capable and wind up in the situation we're in now.

So that would just be a suggestion that I think would be relatively easy to achieve. However, depending on the outcome of the investigation, NRC might suggest that it become a requirement, depending on the specifics. Just my two cents.

CHAIR MALMUD: Dr. Guiberteau.

MEMBER GUIBERTEAU: Mickey Guiberteau. I understand and sympathize with what Dr. Welsh is saying. On the other hand, a bit of that presumes that this is what's caused by user error and we don't know that. And I think before we get into writing new regulations for our licensees that we also take into consideration that this device has been used safely without significant breakthroughs or other findings over the past 20 years. We use technetium generators and we have the same types of regulations that we have now.

And I think before we decide that we need another layer of record keeping, and again, if it's voluntary, I'm all for that. I think some of those suppliers should keep these for their own benefit. On the other hand, I think we need to be careful before we put new regulations on the table until we find out what the results of this investigation are. Thank you.

CHAIR MALMUD: Thank you. Other comments? Yes, Dr. Zanzonico.

MEMBER ZANZONICO: It seems that -- it still seems that if the QC were done, this breakthrough would have been found at the time. So even if it were a product defect would precipitate and

not use error or any such thing as that, it would have been found prior to administration of the rubidium to the patient.

So either there was -- it was not done at the point of service, it was done improperly, or it was done and the results ignored, the out of tolerance results ignored. The result may have been because of a product defect, but regardless of the root cause, it seems less likely if there is a named individual at the site who was certified and in effect, personally responsible for the disposition of the results of those tests in terms of whether they're out of tolerance or not or some such thing as that.

And I'm with you 100 percent. The fewer regulations and the less paperwork, the better. But it seems like there's a breakdown at the point of service. And perhaps with the product as well, but a breakdown at the point of service that could have and should have been revealed if the proper QC were followed and the QC results handled properly as well.

MEMBER GUIBERTEAU: Mickey Guiberteau. Is it the case or is it the current belief or are you able to comment on this, that these incidents would or should have been reported based on the QC of the eluant from the generators before administration?

MEMBER SULEIMAN: Let me mention one fact that I know. The State of Florida, if there's a breakthrough, it's a reportable incident to the state regulator. I was told that early. So they said if they had breakthrough and they didn't report it to us, it's a problem. That's all I know.

MEMBER GUIBERTEAU: But my question was specific to these incidents. Is it the belief if the QC had been done and done properly and I have no reason to believe it wasn't, that this would have been a -- these would have been preventable incidents given that the exposures were not to the level that the NRC needed to be or the state needed to be informed?

MEMBER SULEIMAN: If I interpret your question correctly, yes. I think if the breakthrough testing was done properly no patients would have been receiving contaminated product. And if breakthrough occurs, they're also supposed to report this to Bracco. So if the system -- the system is not broken. The system is just not being executed properly.

And so -- now why the breakthrough wasn't done or whether the breakthrough was done improperly, whether there was confusion, whether there were other compounding factors which I believe exist, I don't think it's going to be A or B. I think you're going

to find there was problems with A and B and there may be some other extenuating factors that are going to play into this when all is said and done.

So how to you execute? So you qualify people. You regulate the product. You regulate the manufacturer. Ultimately at what point periodic mistakes are acceptable? Is this an epidemic or is this just a few isolated cases that are going to turn out to be just isolated?

DR. KREFTING: Ira Krefting. I think there's insufficient data to fully answer your question. And I'll back it up by saying that -- by making reference to the survey studies that perhaps are ongoing or in the process of being initiated. For example, if sites around the country where there was no breakthrough reported, if we surveyed patients there and suddenly we find that there's contamination in these patients, we look back at the records and it looks like QC was done properly, then perhaps we can conclude at that juncture that the QC procedures, as outlined, are not adequate.

Hopefully, we'll find that there are no other contaminated patients around the country, if you wish, the sites we referred to today, one or two rogue sites where things were scribbled down perhaps, these

are all hypotheses. Then, we can make another conclusion. But right now I think there's insufficient data.

MEMBER GUIBERTEAU: Mickey Guiberteau. Just to comment on that and again to reiterate, since there is insufficient evidence and since we are in a discovery period, I think that the assumption that we need to impose new regulations on the quality control of generators, in general, not just rubidium, that is premature.

CHAIR MALMUD: Thank you. Dr. Howe, you wanted to make a comment? And then Dr. Langhorst.

DR. HOWE: I was just going to comment that I'm not sure at this point we have a comfortable feeling that if we go in and see that the quality control was done and they indicate they know how to do it and they did it according to the package instructions, that we really have a number we can trust.

CHAIR MALMUD: Thank you. Dr. Langhorst.

MEMBER LANGHORST: Thank you. Sue Langhorst. I have a logistical question. When a product manufacturer voluntarily removes their product or recalls their product, what are the criteria -- once that manufacturer proves to themselves that their

product is as it is approved -- I mean what's the logistics? How does it come back to market?

DR. KREFTING: Okay, well, we have to, meaning the FDA, have to be assured and be convinced by the manufacturer that the product is now safe and effective and that the safety issue that led to the recall has been rectified and that any corrective action such as a change in the label, a change in the manufacturer have been instituted. So there are a variety of steps.

This also has now been more codified through the legislation I mentioned to you a little earlier in the discussion, the FDAAA Act, in that we can make certain contractual requirements, post-marketing requirements that would constitute actual studies or things that have to be done in terms of a contract to assure all the statements I just made to allow the product to come back to the market.

So the manufacturer has several steps. Sometimes if it's just a lot, one grouping of products, one manufacturing run that's a problem, that's kind of an easier situation. This is much more complicated and we have to be assured of certain -- with a certain degree that all the various questions we've mentioned today are fully answered. Is the

product manufactured correctly? Are the labeling instructions adequate? And has breakthrough going on and we've just not been measuring it over the last 20 years.

In answer to some of the other questions that were brought up by the other panelists a few moments ago, certainly more regulations, more requirements of people are onerous and probably lead to more confusion. If we feel though that there's some specific problem with the product that can be rectified by various options that we have available under FDAAA, there's a term called elements to assure safe use which means that we at the FDA can restrict who actually uses the product.

We have REMS, Risk Evaluation Mitigation Strategy. We can institute REMS. When and if it comes back that this agent is back on the market, we can put it back on the market with a variety of regulatory options for safety. If it has nothing to do with the certification or training of individuals, well, then we don't have to worry about that. But we have these options available to us.

MEMBER LANGHORST: Thank you.

CHAIR MALMUD: Any other comments? Well, we appreciate both the leadership of the FDA and the

NRC in bringing the matter to our attention so that we're informed about it and we look forward to the first step which will be the identification of the source of the problem and then a resolution to it.

Are there any comments from members of the public that we -- I see none. Therefore this session is ended and we will regroup after the break promptly at 10:30. Thank you.

(Off the record.)

CHAIR MALMUD: Thank you, all. We will get started with the second session of this morning's meeting. And the speaker will be Angela McIntosh, who will be discussing ACMUI's 2008 recommendation revision to the Medical Event Abnormal Occurrence Language. It's Tab 14 in your folders.

Angela?

MS. McINTOSH: Thank you, Dr. Malmud. Good morning everyone.

We presented some draft abnormal occurrence criteria back in 2008. And the Committee at that time voted on it. But we couldn't go forward with it and do anything with it immediately because we had direction from the Commission that the existing criteria that had just been approved in 2006, we needed to gain a certain amount of experience with it

before we could open it back up for possible revision.

And so now that we've gained that amount of experience with it, we are ready to open those criteria back up again and revise them. And hopefully make them better, so -- but since there's several years that have expired since these particular preliminary criteria were approved by the Committee, we thought it would be best for us to bring it back to the Committee and make sure that you were still okay with it. So that's really the purpose of this presentation today.

And -- okay -- there we go. Let's quickly define AO, abnormal occurrence. It is an unscheduled incident or event that the NRC determines to be significant from the standpoint of public health or safety. That's the definition in Section 208 of the Energy Reorganization Act of 1974.

So back in 2008, we discussed a couple of things concerning the criteria. First of all, that medical AOs dominate the list of AOs that we submit to Congress every year. And we weren't sure that that was appropriate. It didn't seem appropriate that so many medical AOs were dominating the list because of the second bullet point that most were not really medically significant.

So what I included on these next couple of slides is just for your information. We don't really need to go into any detailed discussion of this. But just for your information what the current criteria -- how they read. There are several, you know, several parts to it.

Now the proposed criteria are much shorter and much more significant. The proposed criteria that the Committee approved in '08, we kept the criterion it must be a medical event first but it has to result in death or a significant impact on patient health that would result in permanent functional damage or significant adverse health effect that would not have been expected from the normal treatment regimen as determined by a physician, either an NRC consultant physician or an agreement state consultant physician.

And so with that in mind, that's the end of my presentation.

MR. LUEHMAN: Mr. Chairman? If I could just make one comment?

CHAIR MALMUD: Mr. Luehman, yes?

MR. LUEHMAN: Jim Luehman. Yes, just for the -- Angela touched on it just really briefly but hopefully everybody caught it that this in no way changes the medical event criteria. We still have the

medical event criteria that are in Part 35. And AOs have traditionally, you know, been a subset of -- a subset in the medical area of the medical event.

So we still have the criteria. For instance, the one that we talked about today in our discussion of the strontium breakthrough, the real question is how big is the subset? How big of a subset of those medical event criteria are going to fall into this upper criteria called an abnormal occurrence, which is something that the NRC is required to report to Congress?

So I guess I just wanted to make it clear to the Committee that by changing these AO criteria, we're in no way changing the medical event criteria where the licensee has to report to the NRC and the agreement state on those and that the physician and/or the patient have to be notified when there is a medical event. Those still stay the same.

The real question becomes by changing these criteria is of those medical events, which are significant enough to meet the threshold of requiring reporting to Congress?

CHAIR MALMUD: Thank you.

Can you give us an example of a medical event -- a generic medical event versus an AO?

MS. McINTOSH: A generic medical event?

CHAIR MALMUD: Well, say someone receives excessive radiation would be a medical event. If someone receives excessive radiation that results in a physical change, such as a burn, a fistula --

MS. McINTOSH: Okay.

CHAIR MALMUD: -- that would be an AO?

MS. McINTOSH: No, no. currently -- the current criteria is it gives dose thresholds. And the vast majority of the time, we never -- there's never any reported or recognized observable effect as a result of these thresholds having been met.

So, you know, we start out with a medical event, you know, for instance the written directive was not followed. And 20 percent -- greater than 20 percent of the dose was given. So if that happens and then there was 10 gray or 1000 rad to -- let's say that the wrong treatments -- the wrong area of the body was treated -- well, if that area of the body received at least 10 gray and a dose greater than 50 percent that was prescribed by a physician, we could stop there.

If those two things happened, we have a medical event. I mean an abnormal occurrence. That's all it takes.

CHAIR MALMUD: And how many AOs did we have last year? Or the last year for which there is data available?

MS. McINTOSH: Going from memory, it was about ten -- ten medical.

CHAIR MALMUD: So it's a small number.

MS. McINTOSH: Relative to -- I'm sorry, go ahead.

MR. LUEHMAN: Sorry, Jim Luehman again. It's a small number relative to the number of medical events. But relative to the number of other events that we report to Congress, it's very large. So the implication, if you're just a Congressman that doesn't know much about the NRC, you would -- I think that one of the things that we're looking at is well, ma'am, the NRC is always reporting all these problems in the medical area to us. But there's none of these -- no reactor events, no industrial events, no research events meet these criteria. But over and over it's the medical event.

And so there's two questions, you know, are we in the right place? And, in fact, the medical area is having problems. Or are the criteria not set right such that we're over reporting what may be, like I said, medical events but are they really significant

enough to rise to the level where they should be reported to Congress?

And I think that we've concluded -- I mean I think the Commission and the staff have concluded that as Angela said, basing it purely on dose is probably the wrong level to report to Congress because the immediate question we get back is okay, well, did anything happen to the person that got that amount? And the answer typically, historically has been no. They will be monitored but then the results are usually, you know, negative at least for the -- I mean obviously you can't look out 40 years what that exposure might do but at least for the foreseeable time, it wasn't.

So the real question is, are we giving Congress information that's useful to them? And that they need to know? Obviously death or serious injury was directly resulting is probably something that they do want to know about.

CHAIR MALMUD: Thank you.

Dr. Langhorst?

MEMBER LANGHORST: The ten that you said that you had for last year, would any of them have met the proposed criteria?

MS. McINTOSH: No, absolutely not.

MEMBER LANGHORST: Okay.

CHAIR MALMUD: Steve Mattmuller?

MEMBER MATTMULLER: Yes, just for the record, I did actually dig up some of the reports. And in 2009, there were nine AOs and they were all medical. And in 2010, there were 15 actually. But they, too, were all medical. So as you said, Congress has this disproportionate view of the problems that the NRC has -- that there appears to be problems in medical and nothing with reactors, which clearly isn't an accurate picture. So, yes.

And then I suppose at some point do we need to make a recommendation to re-recommend our 2008 advice to the NRC as far as how to revise the AO criteria?

CHAIR MALMUD: This is the proposal that Angela is presenting to us. And I think we'll take your statement as a motion to approve.

MEMBER LANGHORST: I'll second.

CHAIR MALMUD: And Sue seconds -- Dr. Langhorst.

Further discussion of this?

MEMBER ZANZONICO: I just have a question and I know this is not within the purview of the NRC because it's not byproduct-related. But, you know,

there was a well advertised occurrence at Cedars-Sinai in California where subjects undergoing head CTs for profusion studies received overdoses to the scalp where they actually got -- lost hair and so forth and so on.

You know it's not clear whether or not that has long-term health implications beyond, you know, cosmesis and so forth. But would -- if that were byproduct -- if such an occurrence as that were byproducts-related, in your estimation would that fall within the criteria of the proposed AO?

MS. McINTOSH: It would seem to fall within the language that says significant adverse health effect that would not have been expected from a normal treatment regimen.

MEMBER ZANZONICO: Because my only concern is that, you know, I agree in principle with this. I just want to make sure it's not such a high bar that significant occurrences, you know, are not missed all together.

MS. McINTOSH: Well, we do -- continuing on with that language, it does have the caveat that this determination must be made by a physician.

MEMBER ZANZONICO: Okay.

CHAIR MALMUD: I think we are all

supportive of this. But I have another question. And that is there was a case that was publicized last year of a man who developed a fistula between his bladder and rectum as a result of brachytherapy seeds going astray.

Would that be considered an AO? It's a permanent -- in a sense he had a permanent anatomic change as a result of that.

MS. McINTOSH: Well, if such an event came in to us, I think that our immediate reaction would be yes. But would a physician -- is a physician willing to make that determination?

I mean I guess the one thing that could go wrong, if you will, is if we get these types of events and then no physician will make the determination for whatever reason. Then a technicality would keep us from reporting it to Congress.

And so -- I mean as long as doctors are willing to make that call, then I think we're okay with reporting what is, you know, medically significant.

MR. LUEHMAN: Dr. Malmud, the other thing I would add though is again these criteria are, you know, the ones where we have to make specific reports to the MEU, to Congress, but keep in mind that we also

-- I mean we also do an end-of-the-year evaluation of the NMED data that is available not only to Congress but to the Committee and anybody that wants to read it to the public.

And, in fact, members of our oversight Committees in Congress have asked us many questions on those medical events. My point being that by raising the AO criteria for what has to be reported in an immediate, you know, and call that as an individual event doesn't mean that the information on those events that may not quite make that cut aren't available. And, in fact, aren't looked at by the members of Congress who have oversight responsibility on the NRC. And, in fact, we've gotten lots of questions related to those events.

So I guess I would add that, too, that not that this doesn't mean -- because these criteria are, at the end of the day, you know, going to be subject to judgment, it doesn't mean the ones that clearly meet the medical event criteria are not going to available or known to Congress should Congress or a member of Congress want to review what's going on in the medical area at the NRC.

CHAIR MALMUD: I don't mean to belabor the point, but I guess I will. In one of the incidents

from last year, the physician didn't report the untoward event. And if I had been a member of Congress, I would have wondered why I was reading about it in the newspaper. But I was not informed about it through the NRC or the VA system.

MR. LUEHMAN: And I think one of the things -- and this is a little bit -- I think one of the things that we've struggled with between our office and the Office of Research, which is responsible for making this report is, I think one of the issues that was involved with that event was how to handle events from prior years that were not properly reported.

Because the AO criteria is supposed to reflect the events that occurred in the last year, the presumption is everything was reported when it should be. One of the problems that you run into is and one of the debates that we have is should we discover an event that occurred in 2005 or 2004, even if it met these criteria, at the time we may have made the report but now the question becomes is now that the report is discovered or the issue is discovered and that patient how has had six or seven years of maybe good health, they've recovered, one of the questions you would come into is, is there a need to report it, you know, six or seven years after the fact

or five years after the fact.

So one of the artificialities of any reporting system is the presumption that everything this done perfectly when it should be done. When we go back and discover events like we have in the brachytherapy area, there is a lot of discussion about the utility and exactly what the proper procedure should be to report those old events and make sure that Congress and the readers of the report understand that these are historical events and not events that occurred within the last year.

And sometimes that is a difficult issue to convey because people just say oh, there was, you know, 25 medical events. Well, yes, but read, you know if you read the report, you know, in fact many of them could have occurred a number of years before.

So that -- I know that doesn't directly answer our question but that is one of the issue that we struggle with. And one of the reasons that may be there are some events that in the past would have met criteria but don't then subsequently get reported when -- in the current year report.

CHAIR MALMUD: Dr. Suleiman?

MEMBER SULEIMAN: Have you considered deterministic effects? I mean Dr. Zanzonico kind of

leaned that way when he was talking about the COMMITTEE hair loss where the hair loss was a deterministic effect. It's an acute -- it's a shorter term, more serious. I would think that would fall under number two.

MS. McINTOSH: I would think so, too. I mean but we could -- to make it absolutely clear, I mean if the Committee thinks it's, you know, prudent, we could add that actual phrase in there -- deterministic effect.

MEMBER SULEIMAN: Now obviously in cancer treatment, some skin erythema is expected as part of, you know -- so I would that's where your definition would address that.

MS. McINTOSH: Okay.

MEMBER SULEIMAN: It would address that.

MS. McINTOSH: It would not have been expected from the normal treatment regimen. So if erythema would be expected from that particular treatment regimen, then it wouldn't be.

MEMBER SULEIMAN: Yes.

CHAIR MALMUD: Laura Weil?

MEMBER WEIL: Because these criteria are relatively subjective and the determination is made by a physician, can you explain to me who is this NRC or

agreement state designated consult? Is this someone from the same institution as where the event occurred?

MS. McINTOSH: No, it wouldn't typically be someone from the same institute.

MR. LUEHMAN: We have a program, a medical consultant program. In fact, some members of the Committee have served or serve as medical consultant.

And when there is an event in one of the regions and there is a medical event, we have a list of -- a roster of medical consultants that we can go to, to provide us medical advice on a particular -- on that particular event. And that's how we do it.

MS. McINTOSH: Thank you.

CHAIR MALMUD: Thank you.

Dr. Guiberteau?

MEMBER GUIBERTEAU: Yes, I just have a question because I know the NRC is very careful about its language. And I wasn't a member of the Committee at this time. In Criterion 2, if we separate those -- and I understand a significant adverse health effect that would have not been expected in a normal treatment regimen, that's pretty clear to me -- I'm uncertain as to what the intent of the first one is. And is that temporal in the sense that a significant impact on patient health that would result in

permanent functional damage, that if there is a significant impact and it is not permanent, that that is not an event? An occurrence?

MS. McINTOSH: Right. That's -- I think that's correct.

MEMBER GUIBERTEAU: Well, for instance in the incident that was mentioned by Dr. Malmud that, you know, because radiation can cause fistulas, it wouldn't be necessarily unexpected. I mean it could happen and be a known complication. However, if it caused the fistula and subsequently the fistula was repaired, it is not a permanent issue. So would that -- then that would not be --

MS. McINTOSH: I don't think that would meet the criteria. And so what we need to think about is should it meet the criteria. I mean -- and so you are correct. I mean maybe there should be some language added to capture that kind of event.

But, again, we're trying to capture what we are terming abnormal occurrences. If that's sort of effect is -- it doesn't happen all the time but, you know, it can happen, when it does happen, is it abnormal? I mean -- is that something that Congress needs to know about? That this patient developed this, you know, side effect but it was correctable.

I mean that's a bit subjective. I can argue probably not. But somebody can argue probably. Because we know that during medical treatments, sometimes there are side effects. And that's just, you know, that's to be expected. Do we need to tell Congress about that?

MEMBER GUIBERTEAU: But the wording is a little, as a consumer, would be a little bit alarming to me in that if there is a significant impact on my health, why isn't that reportable whether or not it is permanent? I'm just talking about the language here.

And I didn't know the intent of, you know, I think the intent might be better worded here. I mean I understand a permanent functional damage that leads to a significant impact on your health, which makes sense to me. But the other is extremely subjective.

And I'm not saying we need to make this so open that we have a lot of occurrences that really don't need to be reported. But if this -- you know, if the Committee felt this adequately expresses their intent, then I think, you know, I'm still not sure it is explained to me what the intent of this is.

MS. McINTOSH: Well, the intent is to capture truly significant events that --

MEMBER GUIBERTEAU: Well, you've already said it is significant by using the word significant. So it is hard to define this phrase with a word that you have in the phrase.

MS. McINTOSH: Right. But the intent is to -- we think we are not capturing significant events right now. So the intent is to capture significant events. Now that we're in significant event space, you know, what is significant enough to raise to the level of reporting to Congress.

Even if we added language that would capture that kind of event that Dr. Malmud mentioned, we probably would rarely get an AO reportable to Congress. So that's an argument for coming up with something that would capture that kind of event.

MEMBER GUIBERTEAU: So the intent here is to make this flexible enough to meet the intent of really the whole definition.

MS. McINTOSH: Well, the intent is to, you know, to capture what is -- the spirit of a normal occurrence reporting is to report something that is truly abnormal. What we're reporting right now is sort of just routine errors kind of.

MEMBER GUIBERTEAU: Sure. Well, I appreciate that.

CHAIR MALMUD: I think -- Dr. Malmud, I think what Angela is transmitting to us is what the Committee had looked at before. And it was an attempt to separate, if you will, the wheat from the chaff. That there was too much -- too many reports going, which were really no clinical significance to congress. And that was burdensome and also would have hidden some significant events that were in that large number. And this is an attempt to separate out what is significant.

Now the wording that was resolved is the wording before us. And it is the best that we could come to at that time.

But if I may, just for the record, let me give a few examples of what might occur and ask you, or whoever on the NRC, whether this would be considered an AO. Giving a patient treatment for thyroid cancer without a pregnancy test and discovering that she was pregnant. And the child will be born with hypothyroidism.

MS. McINTOSH: Well, that's actually not a medical event because the patient got what she should have received. It's just that no one knew of the pregnancy. That is reportable to us under I think it is 35.3047. But it's not -- that wouldn't be -- if

you can come up with a different one, that wouldn't actually be a medical event.

CHAIR MALMUD: Irradiating a wrong organ.

MS. McINTOSH: So if we -- irradiating the wrong organ as a result of that, I mean is it essentially not really a big deal? I mean we know that to a patient, it is always going to be a big deal. But from a clinical significance stance, is that something significant enough to report to Congress?

Maybe I can -- if I can read something here, it might help the Committee out a little bit --

CHAIR MALMUD: Thank you.

MS. McINTOSH: -- that actually our attorneys forwarded to us not too long ago just clarifying the AO criteria, what it is meant to do, saying that if -- the AO criteria are trying to capture things in which the level of protection of public health and safety has been impacted.

I mean so is the level of protection -- when we look at a medical event and something went awry, is that -- did something to awry to the degree that it can be stated that the level of protection of the public health and safety has been negatively impacted? Or did it just -- was there just a little

error which you wouldn't be able to make that statement?

And do these draft criteria capture the idea that the level of protection of the public health and safety have been negatively impacted? I think they do.

CHAIR MALMUD: Well, thank you. There were other comments. I'm sorry, Dr. Thomadsen?

VICE CHAIR THOMADSEN: I have actually the same comment I had in 2008 I think, that it strikes me that Criterion 1 is contained in Criterion 2. And that death is certainly a significant impact on the patient's health.

It also seems to me that the first clause, the significant impact on the patient's health, would be contained in the second cause as significant adverse health effect. And the whole criteria could be started with the -- right after the or in the second criterion.

CHAIR MALMUD: Dr. Welsh?

MEMBER WELSH: So I appreciate all the comments that I've heard so far. And I would like to maybe follow up on some possible wording changes that are based on what Dr. Malmud has said regarding the pregnant patient with iodine-131, which in my personal

opinion, properly does qualify as something serious enough to warrant the abnormal occurrence appellation.

But it doesn't -- it won't because it is not a medical event. Therefore, perhaps the term medical event or reportable event that results in one and two might be advisable to capture that good example that I think you provided.

MS. McINTOSH: Can I clarify something? That type of event would be a normal occurrence but not with the medical criteria. I'm sorry, I didn't make that clear. It would be under a different criterion in the AO criteria. It would be under human exposure.

So it would actually be captured but under human exposure, not under medical.

CHAIR MALMUD: Would it be reportable to Congress?

MS. McINTOSH: Yes.

CHAIR MALMUD: Thank you. The purpose of my question was I understand what our goal was with this. And I'm not in disagreement with it. I just don't want to put members of Congress in a situation which would be embarrassing to them in having to learn about these incidences in the newspaper rather than through the NRC or other appropriate channels.

Mr. Steve Mattmuller?

MEMBER MATTMULLER: Yes, actually in 2009 there were two AOs where they involved patients, who had pregnancy tests that were negative, were administered the I-131 then shortly thereafter were found out to be pregnant. So those have made it to the current system.

But fortunately because of the age, the risk to the embryo because of its underdeveloped thyroid gland, there was minimal risk to the embryo at that time.

MR. LUEHMAN: Mr. Chairman, can I make a suggestion?

CHAIR MALMUD: Yes, please.

MR. LUEHMAN: What I'm going to do is I'm going to ask the staff to go back and get the discussion, the Committee's discussion on these words to see if, you know, in fact the Committee itself from back then can give us some insights on exactly why they liked or didn't like some of these words.

And maybe I think that can inform the discussion a little bit better. So I guess I would -- if we've got time in the afternoon or a little bit later, we could probably revisit this and do -- I think probably do this a little bit more efficiently

than trying to figure it out just by looking at the words that we have in front of us.

CHAIR MALMUD: Thank you for that suggestion. Is that acceptable to the Committee?

(Chorus of yeses.)

CHAIR MALMUD: The Committee finds it acceptable. And thank you for the recommendation.

Thank you, Angela.

MS. McINTOSH: Thank you.

CHAIR MALMUD: Good to see you again.

MS. McINTOSH: You, too.

CHAIR MALMUD: The next item on the agenda is Dr. Donna-Beth Howe, who will be discussing the status of medical events for the Fiscal Year 2011. We appreciate your ability to be here a little early for this session.

DR. HOWE: The first that I'd like to say is that this is a work in progress. We have not completed FY2011 yet.

And so I will have to do an update to the NMED search that you receive as part of the basis for doing the ACMUI review, important things that come out of the medical events. So that will be revised once the fiscal year is over and we've got all the medical events reported.

Where am I pointing? That's as good as any. One of the things I like to do each year is to show you where we've been. So I included both the medical event information for the current year with that of the past year.

And the first thing that probably pops out to you is that in FY2010, we had 49 medical events and now we've got 58. And you're going where are all these extra medical events coming from.

If you're in one group, you may think it is coming in a certain place, like 35.400. But that's not the case. The case is that we're getting more -- we got more medical events in 35.200 and in 35.1000 this year than we did in previous years.

Okay, 35.200 are the imaging and localization. So those are your diagnostic nuclear medicine procedures;

35.300 are your -- we call it procedures that require a written directive with unsealed material. Those are basically your therapeutic but there is one diagnostic procedure in there;

35.400 are your sealed source manual brachytherapy administrations;

600 could be a gamma knife procedure. It could be a high dose remote after loader procedure.

It could be a teletherapy unit procedure. Those are your sealed sources with very high activity giving very high doses in a very short period of time;

And 35.1000 are those devices or sources or it could be your pharmaceuticals that don't really fit into another category. And so we've put them in what we originally call emerging technology but they've stayed there a while so it's other category. And most of those are therapeutic things. And we'll get into more detail on exactly what we're looking at.

So in the next slide, we're looking at the diagnostic medical events. It is very difficult to have a diagnostic medical event. And you're going to see three of them. And some of them are pretty interesting.

The first one is they prescribed I-123 and we've seen cases before where they've prescribed I-123 and by mistake, they gave I-131. This one is even more interesting than that because they prescribed I-123, they got I-123, and when they gave the capsule, the capsule happened to be contaminated with I-131.

And they believe contamination came from the vial cap. And so they ended up giving 380 centigray or rad to the thyroid of the child in this case. So this is a very unusual medical event for us.

The second medical event, they intended to give 123. They gave I-131. They intended to give 5 millicuries of 123. Instead they gave 5 millicuries of I-131. So they gave the same activity but they gave the wrong isotope.

And then the third one, this is another very interesting one. If there were errors that could happen, it happened in this case.

They had an indium-111, which is a diagnostic procedure. They had the material. Unfortunately, they also had a syringe of strontium-89 from a procedure that was supposed to be given about a month before. The strontium-89 dose had expired but it was still in the department. And they picked up the wrong syringe and gave strontium-89 to the patient. And they got 63 rem dose to the bone marrow on a procedure that should not have given you anything to the bone marrow.

The only thing that they lucked out was that the dose had decayed or it would have been much worse otherwise. To those are our three medical events for 35.200 imaging localization.

Now looking at the therapeutic doses, generally we have therapeutic medical events with I-141. Every once in a while, we'll end up with one of

the other therapeutic isotopes. And in this particular year, we ended up with several.

We've got a total of six medical events. Each one of these medical events up to this date has involved a single patient. So we don't have any multiple patients. In this particular one, we've got two patients. They were treated for cystic craniopharyngioma.

And the medical facility believes that the pharmaceutical that came in was mislabeled and that it actually had a lot more activity in it than was on the label. And what made them think that? Well, when they looked at the drainage around the cyst, they found inflammation from radiation type of injury.

And they realized that they had a problem there. They went back and calculated what they had expected to give, 30,000 and 20,000 rads and these patients got 56,000 and 50,000 rads. So well in excess of the medical event reporting requirement. And they believed it was due to the manufacturer not providing adequate measurement information on the label.

We also had a samarium-153. In this case, it was a delivery problem. The syringe was connected to a three-way stopcock. They removed the syringe at the wrong time. When they removed it, they lost some

of the material.

They put the syringe back on and they continued with the delivery. But instead of giving the 25 millicuries, they gave 14, almost 15 millicuries. So that was a medical event.

And now we get into our oral sodium iodides. We've got some typical events here. And we also have a not-so-typical one.

The first one I think is kind of important. Every once in a while, we end up with things that should be medical events that aren't medical events. And we also end up with things that shouldn't be medical events but are because of technicalities.

In this case, they received 25 millicurie I-131 dosage from the pharmacy. The physician looked at it and decided based on the patient that that was an acceptable amount to give, even though the prescribed amount was less. No, it was supposed to be 25, they measured it, it was closer to 20. That's 20 percent low.

And the physician looked at it and said well, okay, I think we can give this. But he didn't change the written directive and they went ahead and gave it. So it became a medical event because it

departed from prescribed dose.

The next one we have the wrong patient. In this case, they were supposed to get 20 millicuries. Instead they got 100 millicuries because that dose was supposed to go to another patient.

We've got the third one. It's one of our typical cases with I-131. The dose comes in two capsules. The capsule is in a vial. The patient gets one capsule. They don't realize they've got the second capsule still stuck on the bottom of the vial.

The third one is one where they prescribed two millicuries. Actually what they gave was slightly less than that. And enough less to be a medical event. And they didn't realize they had the medical event until they did an audit later.

So that concludes our unsealed material, our radiopharmaceuticals.

And now we move into the 35.400, which is your manual brachytherapy. And you'll see we've got 26 medical events. We've got two that are undetermined. One of them was a bilary duct. In this case, 25 of them were prostate and then two undetermined were prostate.

So if we look at the bilary duct medical event, it's the iridium-192 ribbons or seeds in a

strand. And they were supposed to give 20,000 rad. They gave 124 because the positioning, the guide wire that was putting this into position moved five centimeters. So they gave the treatment to the wrong site.

And now we get to the prostate medical events. In this case, we've got 81 patients because we had eight licensees with multiple medical events. The first two are from the state of Kentucky. And the medical events are attributable to the same physician.

So we have 35 medical events at one facility and three at another. The remaining medical events, most of those are going to be coming from just a few states. Wisconsin is one. And if we look at the reasons, well in the first group with 35, they had poor records. Even though there were written directives, they didn't keep the written directive records beyond the three years. And so there's questions there.

They had no post-implant COMMITTEE images. They had not post-implant doses recorded. And they had just a lot of record issues.

You also had, especially for Wisconsin and some of the other states, the states are now looking to see if licensees are comparing their

administrations to the medical event criteria. In many cases, folks were not. But even though they weren't comparing them, most folks didn't meet the medical event criteria but a few patients had a few patients that did.

We had poor image quality post-COMMITTEE as a reason. We had -- and I'm not sure how to interpret this and I think you'll have fun with this one, getting additional information on it -- clinical limitations of the techniques and they are working on improving the processes. That's pretty obscure to me. So you'll probably want to look into that one.

And then we had a number where no reason was given. They just had medical events.

Now let's look at the other 17 licensees. In this case, we're looking at single-patient events. Our most common reason for medical events are sub-optimal dose distribution, poor placement, poor visualization, incorrect identification of the prostate.

We had three where the tumor volume increased due to edema. We had two where there was an underdose to the prostate but no definitive reason given. We had one of our Air kermas again where people are ordering in one unit and receiving

materials in another unit and not doing a close check to make sure what they have received.

We had one case where when they're treating the prostate patient, they may give a combined external radiation and prostate. And if they do that, then they give a partial dose with seeds because they've already given an external radiation dose. In this case, they wrote the written directive in such a way that they got confused and instead of giving the partial treatment dose, they gave the full treatment dose as if the patient had received no external radiation.

Then we had a really interesting one. The patient came in -- no, the patient cancelled an appointment and made another appointment about a month later. The facility had the seeds from the first appointment and they ordered new seeds for the second appointment.

And when the patient came in for the second appointment, they gave the seed from the first appointment, which had decayed significantly. So there were actually two sets of seeds for one patient. And they gave the wrong set.

And then our last medical event was an anatomical issue where it was difficult to deliver the

seeds and the physician stopped the procedure before very many of the seeds were delivered.

The undetermined cases, we've kind of put a hold on looking at our medical event issues that are coming in through our technical assistants for the regions. And so those are undetermined at this point. But we're expecting to get back and make our determination on whether these two licensees with over-exposures in either patients were medical events or not.

Moving on to our other therapy --

MR. LUEHMAN: Donna-Beth, before we leave that --

DR. HOWE: Yes?

MR. LUEHMAN: -- I think the one thing that needs to be clarified with that reporting, again I think Donna-Beth touched on it a little bit but in some of the cases that were reported this year that we considered, those were due to retrospective looks that some of the agreement states -- I think she mentioned Wisconsin did -- and looked back over a number of years.

So while the events are being reported this year, the actual occurrences occurred over a number of the previous years. So it's not like -- I

1 think we'd want to give the impression that Wisconsin
2 or any of those states that are doing the
3 retrospective all of a sudden had a big group of
4 events in this most recent year.
5 The second thing is I would say about
6 those events, in those retrospectives pretty much what
7 we've seen is that, you know, they are spread over, as
8 the list indicated, a number of hospitals had one or
9 two events over a couple year period. The one
10 exception to that is in the state of Kentucky. They
11 did report a large group of events at one hospital.
12 And as Donna-Beth indicated, involving one physician.
13 So that is a group that the state of Kentucky is
14 taking a look at. And still evaluating as we speak.
15 But I just wanted to kind of give a little
16 bit more context to those -- the numbers that were
17 displayed because although they are coming to our
18 attention, and again this sort of goes back to a
19 little bit of the discussion that we had under AO
20 criteria, reporting previously unreported events that
21 may go back a number of years can kind of appear to
22 skew the data.
23 And but, you know, they are being reported
24 now and we are discussing them now because some of the
25 underlying causes, as Donna-Beth said, can be

important. But I just wanted to give that context to those slides on the reporting.

DR. HOWE: And one of the things that I do when I'm doing my medical event report to the ACMUI is I look at the events that are reported in a fiscal year because if an event was not reported back when it happened for whatever reason, then it would be lost to us as looking at data if we didn't bring it forward to where it was reported.

In some of these cases, you've got current medical events in FY2011. And because of that, there is a retrospective. So there's a combination of things. But I try to catch the ones that are reported in the fiscal year, not necessarily that happened in the fiscal year, so that we have a complete record.

MEMBER LANGHORST: Can I ask --

CHAIR MALMUD: Please, Dr. Langhorst.

MEMBER LANGHORST: Sue Langhorst. One the last one that you were talking about with the anatomy issues --

DR. HOWE: Yes?

MEMBER LANGHORST: -- was it reported because the written directive wasn't updated? Or why was that a medical event if the physician, who I assume is the authorized user, decided not to implant

due to anatomical reasons?

DR. HOWE: He didn't give what was on the written directive. And so it met the definition of a medical event.

MEMBER LANGHORST: Okay.

DR. HOWE: And he did actually -- you know, many times we have medical events and physicians do absolutely the right thing. So a medical event is not a violation. In many cases it is reportable but it is exactly the right thing to do.

MEMBER LANGHORST: Okay.

DR. HOWE: So we aren't making a judgment that that was any kind of an error. And I think that is important to note.

CHAIR MALMUD: Thank you for clarifying that.

DR. HOWE: Now for 35.600, we've got actually three major kinds of devices here. We have the high dose rate remote after loaders where we actually have remote after loaders. Most of our medical events with remote after loaders are with the high dose rate remote after loaders. We have gamma knives. And we also have teletherapy units.

There are very few teletherapy units out in my licensing space. And so we rarely have one of

those. So that's why you're not going to see a teletherapy this time.

And when I look at the -- we had 12 medical events in this category. And I broke them down into the two major devices that are used. And with the high dose remote afterloaders, I've also further broken them down because I think we have seen new products come on to the market. The breast balloons, some are mammoSites, some are not. And then we've seen a new device coming on, the Savi 8. And we seem to have a number of issues with those devices. And I didn't believe that they really need to be in the mash of everything else. That they kind of show their own issues and problems.

And we also had some bronchials which we don't have a lot of those but we do have a few. And the gamma knife, we had two medical events.

So for the Savi 8, we had a total -- we had four medical events with a total of 15 patients. Our biggest problems were default settings that were not changed. In one case, they didn't reset the default dwell positions. So they gave the steps in the wrong location.

In another case, they didn't reset the start position default. And so instead of giving the

dose as it was supposed to be given, they gave the area that was supposed to get dose got very little dose. The area that was supposed to get very little dose got a lot of dose. So you ended up with the wrong positioning there.

We also had issues with catheter length. That seems to be a recurring problem, in this particular case, the wire markers stopped at a point of maximum curvature. And so the licensee thought that was the length of the source -- was at the end of the catheter. But it wasn't.

So they had two patients. And it wasn't until they were treating the second patient that they realized what the problem was. So they weren't giving the dose to the right treatment site. They were giving it to the wrong site because the wire length was reported as being shorter than it should have been.

Okay. Then we also had one in which the source on the guide wire actually punched through the catheter and ended up lying on the skin of the patient. That's something we haven't seen before.

And then we went to the breast balloon, this was more typical of what we've seen before. The breast balloon is normally inflated with a liquid. And sometimes there's drainage of the site and people

go in with needles or other things and drain the site. And in the process, they nick the balloon and the balloon drains.

So in this case, they did not have their COMMITTEE scanner, which they normally use to verify that the balloon is inflated and where it is supposed to be. They used ultrasound instead. And they thought the balloon was inflated but it wasn't.

There was drainage that was observed from the surgical incision. And later they concluded that that may have been drainage from the balloon and not from the site itself. And they discovered the balloon was drained on the next visit so they believe that it gave twice the dose that they were supposed to give on the dose -- on the visit when the balloon was deflated.

In the bronchial one, there's -- many times we have problems with the moving. In this case, it wasn't a question that the source moved. It was that it was put in the wrong position.

And in another case, the dwell positions were misrepresented on the written directive. And when they transcribed it over, they got it wrong. And they delivered more dose in both cases to the larynx region.

Okay. Then we've got six patients that are in other categories. And at three institutions, sixty percent of them where the physicist didn't calculate the effect of the tube on delivering the dose. And so they didn't give the right dose. They gave an underdose.

The other two cases, they had -- with four patients the first time -- they picked up the wrong transfer tube. It was longer than the tubes that they normally use so they ended up with skin reddening.

And then they also picked up the wrong transfer tubes in three out of four of the catheters for the last treatment. And they ended up with an overdose to the skin and an underdose to the treatment site.

Gamma knife, we have both an equipment issue and a human factors issue. In the equipment issue, the computer screen froze so the user could not see the time and immediately aborted the procedure.

The manufacturer came back later and said well, even though the screen froze, the second clock was still working and would have terminated the procedure at the right time so you terminated the procedure too soon. We just, on looking at it, think the physician did the right thing.

He had no way of knowing that the second clock was still working and that the procedure would have been terminated. So based on his observation that the screen was frozen, had no idea what was going on, they pulled the patient out.

The second one, they were supposed to deliver 1,600 rad and they delivered 85. The physicist forgot to adjust the weight factor. And so when they wrote the prescription, it gave the wrong dose.

Now we get to 35.1000. We have a number of devices in the 35.1000 group. We've got the Perfexion. We've got the GliaSite and a number of other devices. But the ones we see the most medical events with are the yttrium-90 microspheres.

We've got two manufacturers. The microspheres function slightly differently for each one. So we tend to separate these medical events out by manufacturer. And they flip back and forth as to which manufacturer has the most medical events. In this case, it is the TheraSpheres. So let's see what they did.

Well, we don't normally see shunting but there was a shunting event in which it appeared as if there wasn't shunting when they did the nuclear medicine procedure. But then once they finished the

procedure, they found a lot of dose down in the duodenum. So they believe they gave 9,000 rads to the intestine tract.

Then we have typical medical events where they give the wrong site. They intend to give the right, they give the left.

We have transcription errors. They didn't compare the activity in the written directive with the amount of activity that they received. So they gave all that they received and not what they should have given.

They wrote the wrong segment volume. So he was calculating let's say for the left side and he used the volume of the center in the right side. So that gave the wrong prescription.

The plunger accidently rotated. And when the plunger accidently rotated, there was a stop in the procedure. The microspheres settled. They weren't able to get the microspheres going again. And so they received less than they were intending to give.

There was a clumping visualization. And we found another medical event that is not in your book -- well, it may be in your book but it didn't make my slides -- where clumping was also an issue. So we have two clumping events and then we have got a third one

that maybe also related to that where you couldn't get the microspheres into the treatment site.

We have saline leakage so only part of the dose was delivered. We had failure of a septum vial and so you didn't receive the full dose.

And then in SirSpheres, we've got three medical events. One was the treatment was terminated early on because of patient pain and only 50 percent of the prescribed dose was given. And another -- and this is a SirSpheres occlusion, they believe the concentration was too high. And they couldn't get the microspheres to go through the catheter and be delivered.

And they tried to increase the volume and that wasn't -- would not move the microspheres. So their corrective action is to dilute their solution down more so that they don't have a high concentration. And then we have one in which the medical physicist read the written directive incorrectly and gave the wrong dosage.

CHAIR MALMUD: Thank you. Are there questions for Dr. Howe about any of these issues?

Dr. Zanzonico?

MEMBER ZANZONICO: Yes, thank you very much for that. That was really very instructive.

I just have a couple of clarifications. I think it was on your tenth slide. Yes, slide number ten, this was a 35.400 prostate.

DR. HOWE: Yes?

MEMBER ZANZONICO: I'm just trying to clarify what the numbers mean because it says prostate 81 patients. And then towards the right, it says 25. And I thought that number referred to the number of events.

DR. HOWE: The number in parentheses is the number of patients that were involved in the 25 medical events.

MEMBER ZANZONICO: So there were 25 medical events but it says 81 patients.

DR. HOWE: Yes.

MEMBER ZANZONICO: So when you say 25 events, you mean sort of by category?

DR. HOWE: By location.

MEMBER ZANZONICO: Okay. I thought it meant the actual individual number. And I'm trying to reconcile those two.

DR. HOWE: No, that's by facility.

MEMBER ZANZONICO: Okay.

DR. HOWE: And as you look down through the list, you'll see that --

MEMBER ZANZONICO: Okay, that --

DR. HOWE: -- there are 3, 2, 6 9, 2, 3 --

MEMBER ZANZONICO: That clarifies it.

DR. HOWE: -- patients involved at a given facility.

MEMBER ZANZONICO: Okay. The other question I had is like it seems that in some of these instances, the medical event or the misadministration is immediately correctable. And I'm thinking, for example, in that case of samarium where the patient was underdosed.

It would seem that within the day -- I men it is an intravenous injection within the day, an addition objection could have been to bring up the total administered activity to what was prescribed. If that were done, would that still be a medical event?

DR. HOWE: Yes. The medical event is when you have something that does not -- is something that meets the criteria of a medical event. The physician can take absolutely the correct action afterwards, can bring the dose up to what the patient needed. But that doesn't negate the fact it was a medical event.

CHAIR MALMUD: Thank you. Other questions? Dr. Thomadsen?

VICE CHAIR THOMADSEN: On your Slide 5, I was just wondering if the facility does any check on the activity before they inject it? Is this not expected?

DR. HOWE: I'd have to go back and look carefully. In our license -- in our regulations, the licensee can verify -- the licensee does not have to verify what comes from the manufacturer. They can use the manufacturer if it comes in as the unit dosage.

And if they have to do any manipulation, they could use a volume and activity correction. I believe in this case, they made measurements afterwards because they accepted the manufacturer’s information. And that's acceptable in our regulations.

And especially for some of these therapeutic radiopharmaceuticals where it is difficult to measure in dose calibrators, we prefer they use the manufacturer's number then think they have the accuracy that they have with technetium because we've seen many, many cases, samarium and P32 especially where they believe they can measure it more accurately on their dose calibrator and then they routinely are 20, 30 percent low. And we end up a whole stack of medical events after that.

VICE CHAIR THOMADSEN: On your Slide 18 --

DR. HOWE: Eighteen okay.

VICE CHAIR THOMADSEN: -- in the first one, the 60 percent under dose, physicist did not calculate the effective tube used to deliver it. What tube is that that has a 60 percent defect? Any idea?

DR. HOWE: Sometimes we have very skeptical information at this point. But we could go back and ask for additional information. This was the reason given that he hadn't calculated that he would lose dose based on the tube he was using to deliver the dose. I cannot tell you any more at this point. This may be one that you want to delve into more.

VICE CHAIR THOMADSEN: All right. I can't think of any tube they'd be using that would drop 60 percent of the radiation. Interesting.

CHAIR MALMUD: Yes? Dr. Suh?

MEMBER SUH: Dr. Howe, thank you for the presentation.

Do you have a sense for these various medical events if these centers are using some type of safety checklist because some of these events that have occurred may have been averted if someone did a time-out to say are we treating the right location, have we calibrated the machine properly, is the catheter in the right position before we, you know,

inject --

DR. HOWE: I think you'll see as you go through the reports in NMED and the reports back from the licensees that in many cases, that's what they're implementing now. They're now saying okay, we're going to have a time-out and we're going to check to make sure of things, which the implication is they didn't have time-outs before.

MEMBER SUH: Sure.

CHAIR MALMUD: Dr. Langhorst?

MEMBER LANGHORST: Thank you, also, for this report. It's always very helpful every year. And each year I understand it more. So thank you.

I didn't go through the reports that you gave us in here, which are very helpful, but can you give me a sense of how many of these are in agreement states versus NRC-regulated states, non-agreement states?

DR. HOWE: I cannot give that to you off the top of my head. I would guess most of them are in agreement states because there are a lot more agreement states.

MEMBER LANGHORST: Right.

DR. HOWE: I know if you look at the prostates, most of those are in agreement states.

MEMBER LANGHORST: I know that our agreement states are challenged with some of their resources that they are able to devote to inspections and so on. I just wonder are -- how does that impact medical events? Are things not being identified soon enough that maybe they would see precursors to a medical event? I'm just kind of asking a general sense of how you feel if there's more issues in agreements states because of challenging resources that agreement state programs have right now.

DR. HOWE: I think with the very low number of medical events that we have per procedures, it would be difficult to make any sweeping statement. I think it may be easier to look and se how many times the inspectors identified medical events and therefore it is an indication that the licensees are not self-identifying medical events and may have issues with understanding the definition and reportability criteria. I think we could get to that a little bit easier than the other question.

MEMBER LANGHORST: Thank you.

CHAIR MALMUD: Dr. Welsh?

MEMBER WELSH: Jim Welsh here. I, too, would like to reiterate the thanks and appreciation for this very comprehensive review. And since it is

thorough and comprehensive, I have a number of comments or questions. And I'll go through them sequentially by section.

The first in Section 35.200 regarding the events involving the samarium-153 and the two iodine cases where there were underdoses. My first comment, again, is a philosophical one that I've mentioned before, that in my personal perspective, these underdoses I don't think should be categorized as medical events.

And I understand and appreciate NRC's perspective that it is important to identify trends, and therefore keep track of underdoses. But since underdoses fall into a different category of potential harm to a patient because they might not cure the patient, I think it should be separate from the other category of harm to a patient, which is caused by direct consequences of overdoses.

Having said that, I think that since no harm was done, maybe it would be nice if there was a separate category such as medical occurrence due to or violation due to under-dosing of radioactive material.

The other point is that these could perhaps have been taken out of the medical event category if there was permission for written directive

adjustments before the patient leaves the treatment area. And I'll get back to that point again when we talk about the Y-90 cases.

Moving on to the 400 series, 81 patients, 25 events is a lot. And I would not say that a lot of these patients were armed by these medical events or the title medical event. But the biggest reason for this many is because of the retrospective reviews that have been conducted.

I think I and other members of this committee have stated on many occasions that if we all went back and looked carefully at prostate brachytherapy procedures, that we would notice that disappoint, perhaps surprisingly high number of perfectly good, clinically good prostate brachytherapy procedures would have to meet the -- would have to be called medical events because of the limitations of the definition.

Specifically, things such as the poor image quality on postoperative CTs, we've stated in this room on many occasions that post-implant dosimetry is challenging. Imaging is difficult and the borders are fuzzy. And for that reason, using dose, especially the D90, is not a very good parameter for defining medical events from a regulatory

perspective.

There were a few underdoses due to -- three underdoses due to edema. And I would argue that they should not be medical events because these might be patient-related changes. The patient didn't intentionally change his anatomy.

But a perfectly good implant may be categorized as a medical event simply because of anatomical changes within the patient due to edema and the timing of the post-implant dosimetry, which artificially gives you a dose calculation that is less than the written directive for the D90.

There were two other that are underdoses for no definite reason. I suspect it is because of the edema. No proof of that, of course, but that would be my guess.

The other one that says anatomy issue, the procedure was stopped because of an anatomical change. And this meets our current definition of medical event. And, again, we know that medical event is not supposed to be a derogatory term. But I think that the average patient has a difficulty with that -- with discerning the difference.

And I do wish that there was something that was a separate category other than the medical

event, which most patients, I believe, think is synonymous with the old term misadministration, which in the average person's mind is a very negative -- has a very negative connotation.

DR. HOWE: Well on the anatomical, there was not anatomical change.

MEMBER WELSH: But did you -- I'm sorry. What?

DR. HOWE: It was -- on the anatomical issue, there was no anatomical change. In other words, this patient wasn't necessarily a typical patient. So there were issues in having to deliver it.

MEMBER WELSH: I understand that.

DR. HOWE: Okay.

MEMBER WELSH: Which leads to the next point which is that if the written directive could be adjusted in some form or fashion before the patient leaves the control of the authorized user, this situation, which the physician probably used good judgment for, which perhaps prevented harm from occurring, would not have been labeled as a medical event.

MR. LUEHMAN: Dr. Welsh, I think that a lot of the comments that you are making were relative

to those -- you can take those up with Mr. Fuller and his report on the, you know, the -- on Houston, on the workshops. And he'll be glad to take any additional comments we have on that.

I mean because I think that, you know, your points are well taken on some of these. I will say that on at least the events in Kentucky, the ones that we've looked at, seen the data on, they're clearly -- they run the whole spectrum from ones where there may be the issues you describe as well as some events which would clearly not be -- which would not be considered standard practice implants by anybody's definition.

So you're right. Our definitions and our consideration of, you know, this procedure, we're working on it, you know. And we had the workshops and we're continuing to move forward on that. So --

MEMBER WELSH: If I might just --

MR. LUEHMAN: Sure.

MEMBER WELSH: -- conclude quickly by saying that the series of events that have been presented, I think by and large prove that the ACMUI's predictions are correct. And, therefore, that the ACMUI's recommendations should be paid attention to. Thank you.

CHAIR MALMUD: Thank you, Dr. Welsh. And thank you, Dr. Howe.

Dr. Howe, I have a question, which came up on Slide 11. And that said some of the licenses had multiple events, including no written directive.

That seems kind of elementary in terms of a deficiency. How could a process be ongoing without an order, a written directive, a prescription, whatever term they want to use?

DR. HOWE: I went back to look to see what that meant. And it meant that they believe there was originally a written directive. It wasn't the fact that there was never a written directive. It was they tossed the written directives and didn't keep them.

CHAIR MALMUD: They tossed them?

DR. HOWE: Yes. The requirements are keep things for three years. So they threw things away.

CHAIR MALMUD: I see.

DR. HOWE: And sometimes they threw things away that were less than three years.

CHAIR MALMUD: Do they understand now what the rules are?

DR. HOWE: I think they're being instructed.

CHAIR MALMUD: Thank you. Are there any

other questions? Any other questions or comments?

(No response.)

CHAIR MALMUD: If not, thank you. Seeing the list with as many of the details as you have was very useful to us.

Thank you.

The time is now seven minutes before 12. So we will break and come back after lunch at 1:30 promptly for the NRC rulemaking workshop with Mr. Fuller.

Oh, excuse me.

MEMBER MATTMULLER: Dr. Malmud?

CHAIR MALMUD: Yes.

MEMBER MATTMULLER: Just a procedural issue. During our discussion of AOs, we had a tape. We had a motion on the table. Do we need to address that? To table the motion, hold on to it until further discussion or --

CHAIR MALMUD: You are correct. We probably should table it because we are going to have a small meeting about the issue. So if you would make a motion to table it, if you care to, or whatever you want to do.

MEMBER MATTMULLER: So moved.

MEMBER LANGHORST: And I'll second that.

CHAIR MALMUD: It's been seconded. All in favor of tabling it.

(Show of hands.)

CHAIR MALMUD: Thank you. Thank you for bringing that item to conclusion.

And we'll break for lunch. Thank you.

MR. EINBERG: We actually have something.

CHAIR MALMUD: Oh, it's another issue? Sorry.

MS. COCKERHAM: If you've completed your financial disclosure forms, could you please drop them off with me? Thank you.

(Whereupon, the foregoing matter went off the record at 11:51 a.m. to be reconvened in the afternoon.)

A-F-T-E-R-N-O-O-N S-E-S-S-I-O-N

(1:28 p.m.)

CHAIR MALMUD: Good afternoon ladies and gentlemen. It is 1:30 and we'll try and keep on schedule this afternoon so that those of you who have transportation obligations later in the day can meet them.

And we will begin with the 1:30 session and that is Mike Fuller. And welcome again, Mike. You

were away from the table for a while but I saw you sitting over here.

And Mike is going to discuss the NRC Rulemaking Workshops that were held in New York City and in Houston.

MR. FULLER: Okay, Thank you Dr. Malmud. Again, I am Mike Fuller. I am the team leader for the Medical Radiation Safety Team here at the Nuclear Regulatory Commission.

The purpose of my presentation today is to provide an overview of the key messages that we received during our Medical Rulemaking Workshops. And as Dr. Malmud mentioned, they were held in New York and in Houston, the first one in June and the second on in Houston in August.

We hosted two very successful public facilitated two workshops this summer and I am going to share with you the key messages that we received during those workshops of the things we learned as a result.

Just as a way of outline what I will go over again, we will talk about the key messages. The day one key messages had to do with the medical event definitions, other things related to the expanded Part 35 Rulemaking we are currently in the early stages of.

We are on day two of each of those workshops so we will go over those key messages that we heard.

In addition, we will -- Well to be specific, the first day was the medical event definitions associated with permanent implant brachytherapy. The second day had to do primarily with amending the attestation requirements and extending grandfathering to certain certified individuals, naming assistant or associate RSOs on the licenses, and additional requirements for molly-99/technetium-99 generators.

I will also go over some of the next steps in the rulemaking process.

A little background. In July of 2010 the Staff presented to the Commission a rule change for amending the medical event definition for permanent implant brachytherapy. The Commission disapproved the Staff's recommendations and directed the Staff to develop a new definition. Specifically, the Commission directed the Staff to work closely with the ACMUI and the medical community to develop event definitions that would do the following three things: protect the interests of patients; allow physicians the flexibility to take actions that they deem medically necessary; and preserve the NRC's ability to detect

misapplications of radioactive material and failures in process, procedure, and training.

If you will recall, we devoted the April ACMUI meeting primarily for the purpose of the discussion of these same topics. We then held our first workshop in New York as I mentioned in June and our second workshop in Houston.

I want to take just a minute to thank the ACMUI for recommending that we shift our second meeting from June to August. If you will recall, Lynne Fairobent voiced some concern, from the American Association of Physicists in Medicine, voiced some concern that there was not enough advance notice provided for our workshops. This prompted some discussion amongst the AMCUI at that time and ultimately a recommendation.

This recommendation enabled us to make a change in our schedule. And the bottom line, I believe, this improved the level of participation that we were able to enjoy.

For each of the workshops we convened two separate panels of experts. For the Medical Event Definition Panel, it included representation from this body, the ACMUI, our Agreement State partners, ASTRO, the American Society of Radiation Oncology, the

American Association of Physicists in Medicine, NRC staff, the Department of Veterans Affairs, representing our licensees, and a patient's rights advocate.

For the second panel, what we referred to as the Attestation Panel, I guess, we included representation again from this body, the ACMUI, the Agreement States, the American College of Radiology, and the NRC Staff.

I want to thank Dr. Welsh, Dr. Zanzonico, and Dr. Langhorst for their participation as panelists on these workshops. Also I wish to thank Dr. Malmud for participating in the New York workshop. Your participation and comments prompted very helpful discussion.

Also, Steve Mattmuller participated by webinar for both of the workshops and Dr. Langhorst participated by webinar for the first workshops and each also provided comments that added significantly to the discussions. And I want to thank everyone for that.

Okay. So what did we hear? What did we learn? Now there is no particular order here but I want to go through some of the key messages that we received from the workshops.

The first thing was among the states we had fairly consistent regulations. And when I say states I mean the Agreement States. But there is wide variance in the interpretation and implementation of the regulations.

Now this message pointed out that there is a real need for inspection guidance and training. And we are currently participating in a working group with our Agreement State partners to address this need and we are working on specific guidance for inspectors for the current rule because we will have to live with it until we get the new rule, hopefully in 2014. We are expecting to a new rule in 2014.

Another key message that we heard is that the medical definition for permanent implant brachytherapy needs to be revised and should be based upon total source strength or activity and not absorbed dose. Now I want to say that there was extremely strong consensus for this position from all of our stakeholders in the medical community. We heard numerous reasons for this position from many people and why they all believe that this is necessary.

We also heard that if the medical event definition is based upon total source strength, that a tolerance of plus or minus 20 percent is a reasonable

tolerance.

We also heard that the term "medical event" should be reserved for those instances where there is real harm to the patient or a potential for same. In other words, the medical event has been reserved for those things that are clinically significant.

We also heard that the term "medical event" is problematic for many stakeholders, especially in those instances where there is no medical consequence. We listened to lot of discussion at both workshops. Some suggested that we go back to a two-tiered system.

Well we also heard another key message and that is that what we call it is much less important than what we do with it.

We also heard that licensees should be trained in the policies and procedures for identifying medical events and that the patient's rights should be protected. The patient's rights advocates that participated in our panel discussions stated very clearly that whatever is ultimately decided, the patients must be kept informed.

We also heard that the authorized users should be required to attest in writing that the

distribution of seeds within the target was implanted as intended. Now this point was made in recognition that with an activity or total source strength basis system or rule there is a possibility that all the seeds could be implanted within the target but bunched up or not as evenly distributed as intended.

We also heard that post-implant imaging should be required.

Okay now moving on to the second day of panel and the second day discussions, we also heard some very key messages there. The first had to do with attestation. We heard that the requirement for attestation for board-certified authorized users, authorized medical physicists, radiation safety officers, and authorized nuclear pharmacists should be removed. We heard that board certification coupled with recent of training requirements should be sufficient for the regulator's needs.

We also heard that there should be no requirement for attesting to someone's competency, but rather preceptors should be attesting to someone's training and experience necessary to carry out one's responsibilities independently.

Moving on to assistant or associate RSOs and whether or not they should be allowed to be named

on NRC licenses, we heard that the NRC should allow for the naming of associate or assistant RSOs on an NRC medical-use license. And we also heard that there should be no arbitrary limit placed on the number that can be so named. The point was made that if we tried to somehow limit or restrict or provide some sort of specific requirements in this area, that it would be hard to apply evenly. There are needs at very large organizations and large medical centers that are not shared by some smaller medical institutions.

We also heard that whether they are called associate RSOs or assistant RSOs is something that we need to exercise some care when we decide what to name these individuals because the actual name associate versus assistant has some connotations within the medical community. So we will be looking into that as well.

Moving on to the molly-99/technetium-99m generators, we heard that there should be a new requirement for testing each elution, not just the first elution. But we also heard that there should not be a requirement for NRC licensees to report failures to the NRC.

So what's next? A few things that are currently ongoing and coming up soon. We are currently

working to develop a regulatory basis for including the medical event definition issue in the expanded Part 35 rulemaking that is currently underway in its early stages.

We are also currently reviewing the regulatory bases that we developed previously for the expanded Part 35 rule to see if there are any needed changes or amendments to those. And we owe the Commission a proposed rule in December 2012 and a final rule in October 2014. And that is based upon our current schedule.

The next slide is the… ask if there are any questions or comments. But before I get to that, there is something I wanted to share that kind of, I guess, speaks to this whole issue of medical event definition and kind of goes back to all of the discussions that had at both the workshops and so forth. And I think it kind of brings it home. I think most of the people that participated in the workshops recognized that there is a need for a strong regulatory framework. It is just a matter of what should that look like and what should it entail and how detailed should it be and how far should it go.

But we had an event reported to us early this week. So it is not even public yet. We have to

hold them for a few days to see how things shake out. So this is very preliminary information and so I won't divulge where it is from or anything. But let me just read to you a short summary and this is recent.

The licensee reported that of the 71 seeds, only three were placed in the prostate. The others were located in the bowel, the bladder, the bladder wall, the lumen of the bladder. The intended dose to the target was 145 gray but the D90 to the prostate was 2.2 gray. The highest preliminary dose estimated to an unintended organ is 49.2 gray to the large bowel.

The patient has excreted eight seeds since the event. The licensee attributes the medical event to the non-use of fluoroscopy and absence of a medical physicist during the treatment. And those were both standard procedures that we used in the past.

So of course this raises all sorts of questions for us as regulators and I don't want to get into the details of that trigger event because that is really all we know. But I wanted to share that with you just to sort of highlight some of the challenges that we, as regulators, face when we are encouraged to do something that is entirely and drastically different than maybe what we have done in the past.

I think again the messages that we heard at the workshops were very, very helpful to us as we start developing our regulatory bases and moving forward in rulemaking. But these types of medical events still become very, I think there always will be instances where these happen and they are reported to us and need to be reported to us so that we can follow-up and help to improve the process as things go forward.

So with that, I will end my presentation and take any questions that anybody might have.

CHAIR MALMUD: Thank you, Mr. Fuller. Are there questions? Comments? Dr. Zanzonico.

MEMBER ZANZONICO: Yes, in the same vein on the question of the medical event or the proposed medical event definition for implant brachy, the proposed definition is based on a 20 percent source strength, plus or minus 20 percent source strength within that prescribed. But then in the next slide it indicated that there would be a requirement for attestation by the licensee, by the authorized user that the seeds were implanted as intended and that there is also a requirement for post-implant imaging.

So in a regulatory sense, what would that be called if the source strength criteria was met so

it wasn't a medical event on that basis, yet either of those other two requirements were not filled? Either they didn't do post-implant imaging or this attestation was not done.

MR. FULLER: Yes, those are good questions. Now keep in mind that these are suggestions, comments, recommendations that we heard at the workshops. We are going to have to take these and use this to develop a regulatory basis and tell our rule makers, the folks that take us through the process of developing a proposed rule. And these are things will consider as we develop that regulatory basis. So we will have to make some assumptions.

But assuming that we end up with a proposed rule but something along those lines, then in my way of thinking, when you are talking about medical events and if in fact we end up with a medical event definition based upon activity, then the plus or minus 20 percent would be one of the criteria that had to be evaluated against the definition.

The other thing which again if we follow specifically the recommendations that we heard, is that these seeds need to be distributed throughout the target organ. Again, we are talking just about the prostates for this particular discussion and they

would -- that there is an expectation that there would be an attestation again, that they were distributed more or less evenly or as intended.

Now whether or not that would end up being a medical event I think is something we are going to have to discuss further and get some clearer understanding of because it is not clear to me that that would automatically -- In other words, I guess what I hesitate to say that that would definitely be a medical event because that is a failure to create some sort of a document.

What if they had, based upon further observation, that they had reasonable distribution? Well we wouldn't want to call that a medical event. So maybe it might be a requirement and that if the requirement wasn't satisfied, then we would look at that and whether or not it should be cited as a violation.

The same way with -- I'm sorry. Let me get back to it. I'm sorry. Help me out Dr. Zanzonico. What was the other point?

MEMBER ZANZONICO: Well I think it was all the same question as the post-implant imaging.

MR. FULLER: Right, post-implant imaging. I'm sorry.

MEMBER ZANZONICO: That was the second requirement.

MR. FULLER: I lost my place there.

MEMBER ZANZONICO: Yes.

MR. FULLER: Yes, again I think and this is just at this point in time, this is really, really early. So these would be the types of discussions that would be going on as we start looking at this.

I think whether or not it would be a medical event would have to be determined based upon the other criterion. But the failure to do post-implant imaging, if in fact that is something that becomes a rule, I think would be something that would need to be dealt with more in the enforcement space, rather than in the medical event space.

MEMBER ZANZONICO: Right.

MR. FULLER: Because again, it would have to depend, in my opinion, and this is just my opinion. I think medical event would have to be tied more to ultimately what did you find out about whether or not things were done in accordance with the intentions of the authorized user.

MEMBER ZANZONICO: I mean, as we have heard this, whether intended or not, there is a pejorative connotation to "medical event." And I think there was

some discussion, though no consensus, at the New York workshop that maybe there is another category, another term that should be introduced where there is sub-optimal management but yet with no significant clinical effect on the patient.

What is the status of that in terms of the NRC's current thinking?

MR. FULLER: Again, all of these are things that we have heard this summer. We are going to take them back. We are going to examine them, develop some regulatory bases-type document. In other words, when I say regulatory basis, that is the way we start the process of getting what we feel like we want in terms of what our needs are to the folks that are working in the rulemaking. And it goes into the rulemaking working group, which tends to sort of polish and work on these sorts of things and develops a proposed rule.

But back to this issue of not having post-implantation imaging and so forth. It kind of reminds of the issue there was something that was very controversial in the proposed rule that was disapproved by the Commission where failure to develop a written directive was going to be called a medical event. That was extremely controversial.

Now again, that proposed rule was not

approved by the Commission and for lots of reasons. But so that is something that is kind of recognized as being very, very controversial.

CHAIR MALMUD: Thank you. Dr. Welsh.

MEMBER WELSH: I was just going to reinforce what Dr. Zanzonico has said, that should things evolve such that the attestation writing by the authorized user that the seed distribution was according to his or her intentions and plan become a requirement, this would be a classic example of why I personally have felt that the term "medical event" would be best left for those events that are truly of medical consequences to the patient; whereas a different term might be appropriate for some violation such as this.

And I'm sorry that I can't come up with an appropriate neutral term. I thought of maybe policy violation as something that would be acceptable. But I do wish that there could be some distinction between something that happens to the patient that could possibly be of medical consequences, versus something such as the authorized user forgot to write the attestation after the procedure and is a violation of the policy.

And I think this would be a good example

of why I personally have felt this way and there are many other examples that I have used in the past but this one is pretty concrete and obvious to most of us.

MR. FULLER: Yes, let me say a couple of things. First of all, with regards to whether or not we have a two-tiered system again, that is something we need to consider as we develop this. We heard it loud and clear in the workshops. We have heard it loud and clear actually in the April meeting as well. And so we will definitely seriously consider that as we draft the regulatory basis.

But as far as what we call it, let us come up with something. Sometimes it is easier for somebody to throw one out there and then we will bring it back to you guys and you all can tear it up for us. You know, tell us what you like and don't like. In other words, we will try and come up with something and see what you all think about it, again, if we get to that point.

CHAIR MALMUD: Thank you. Are there other -- Yes, Dr. Langhorst.

MEMBER LANGHORST: I just wanted to mention it was extremely helpful after the June meeting workshop that, and I know you guys struggled whether you should or should not do this, but you came up with

a summary of the key items that you heard from that workshop for those of us who then attended the second workshop. And I commend you on doing that and I thought that was very helpful in my understanding and kind of summary of the comments that were made for the first workshop. I was not able to hear all of it but I did participate in some.

I think that there is maybe one key message that should be in your slides for our presentation and that is the discussion of the authorized user being able to change the written directive as he or she is doing this procedure and before the patient leaves. I think that is a very important item that is a key message that impacts like the question I asked earlier of Dr. Howe of that one medical event she presented that there was a difference because the anatomical situation did not allow all the implanted seeds.

So I would suggest that you might add that one to your list of key messages.

MR. FULLER: Thank you.

MEMBER LANGHORST: On the RSO, listing more than one RSO, that may not be as needed if we drop the requirement of preceptor statement for those who are Board certified. It may not be quite as needed but

there may be certain licensees that it would be very helpful to have that ability to list more than one RSO, to list the associate assisted deputy, whatever fits their organization.

So while it may not have the same necessity, if that other problem is addressed, I think it should be allowed.

Then as far as the moly/tech generators and the question about whether or not there should be a requirement to report breakthrough failures to NRC, I ask that as you are considering that question, that you think of what other requirements there are in that case. It may not be NRC requirements. It may be FDA or good manufacturing requirements or whatever. And whether NRC's requirements really do apply to those who can fix the problem.

And I know in Houston a lot of us were talking about if the licensee has to report this, we don't have the ability to correct it. It is the manufacturer. And so I just ask you to consider that as you are doing your proposed rule drafting.

MR. FULLER: And if I might. A little bit related but not entirely related, we heard this morning about the issues with the rubidium/strontium generators. So one thing we are already thinking

about, just so you know, is the regulatory basis that we developed for this particular change as part of the expanded Part 35 rule was in response to some very specific things that came up a few years ago. And we are already, at least amongst the Staff, recognizing that perhaps we need to step back from that just a little bit, look a little bit more globally.

We heard a few comments about this in Houston and see if there is not a better way to address these concerns but in a more, like you said, a more generic way. Instead of having some rule changes specifically to a moly-99 generator, we need to step back and look and say okay how can we maybe better address this issue. Because we don't know what the next one might be or other types of generators. Because we don't want to necessarily put ourselves within such a tight box that the next time something happens we have got to go to rulemaking to deal with it. So we are already considering that as well.

CHAIR MALMUD: Other comments or questions? Dr. Van Decker.

MEMBER VAN DECKER: Two, I guess. Number one, just to pick up on the last point you just made because I think this morning's discussion is ripe for growth of the field of new generators down the line,

and I would just point out that a piece of the solution to the Board's question on the last rewrite was to use an appendix to kind of do more with guidance in some things for individual things and to have the rulemaking space be much more specific to construct and then refer to an appendix where you might be able to change things over time as the field evolves and not be so rigid as to where we need to be. Just a thought.

The second comment, I guess I missed Debbie Gilley several times these two days. My usual -- Since I am the one who usually will make the state comment while having the most people affected by this all the time.

You know recognize that, if you get a final rule in 2014 that the States get three years to comply. So everything we are talking about here is really 2017 before we get uniformity around the country. You know part of our goal is many of us training people and sending them to different states would like to have some consistency in what everyone is reporting and how we are training them for what environment they are really going to be in. So I guess my concept was around your slide on the medical event definition that said: "Among the states -- fairly

consistent regulations, but wide variance in the interpretation . . ." I guess, you know, medical event definition needs to be a Category B, right? Everybody should be working off the same definition and it should be clean and tight enough that the interpretation of something that has this much import and this much impact on people's practices and on patients, that the guidance needs to be -- I never heard of compatibility guidance but I mean we should all be looking at the same thing and speaking the same dialect when it comes to something along that lines. And whatever kind of wordsmithing or educational or technical papers it takes and whatever else, we don't want this to look like, I won't say about other continents, but are one nation.

MR. FULLER: Thank you for that comment. It is something we are always challenged by and we do the best we can to deal with it but it is a huge challenge for us as regulators as well.

CHAIR MALMUD: I have a question for you.

MR. FULLER: Yes?

MEMBER VAN DECKER: Are there plans afoot for the next workshop?

MR. FULLER: Not at this particular. For this particular rulemaking activity, thanks to the

ACMUI, and the workshops and what we anticipate to be a continued relationship here, and keep coming back to you along each step of the way, we haven't anticipated further public outreach prior to the proposed rule.

Now that being said, I think it is fairly normal that once we have a proposed rule, and I can't speak for our rulemaking folks, but I know it is fairly common practice that once we have a proposed rule and we have it published for comment at that point in time, we may hold some further workshops on the proposed rule.

CHAIR MALMUD: Thank you. The reason I asked is I know we need a certain number of months' lead time to do an announcement. And therefore, if we are considering another one, we ought to begin the consideration process early so that if it needs to be implemented, it can be implemented with ample time notice.

MR. FULLER: Thank you for that reminder.

CHAIR MALMUD: Any other items on the -- Dr. Van Decker.

MEMBER VAN DECKER: Sorry. You just jogged a question in my mind.

So if the proposed rule is going to be the end of 2012 for the next set of public workshops and

going towards a final, what do you see as the timeline for what ACMUI will hear next spring? I mean, is there going to be a full year of you guys in comment digestion? What is going on in that period of time?

MR. FULLER: Well, I'll have to pull my calendar. You are going to get -- What's that?

MR. LUEHMAN: They are going to get a briefing on it. Right?

MR. FULLER: That's right. This afternoon there will be a briefing on all of that.

But just so you know, because this is medical major -- major medical policy and its rulemaking, you will get 90 days before it actually gets sent to the Commission as a proposed rule.

So early in the process, the ACMUI will have their opportunity to weigh in. And again, when you deliberate on that and discuss it, that will have to be in a public forum. So there are more opportunity, at least for public -- I won't speak for the chairman of the committee as far as participation, but there will be an opportunity for public awareness at the very least.

CHAIR MALMUD: Thank you. Dr. Suleiman.

MEMBER SULEIMAN: I'm not sure if -- We are just listening to the results of the workshops.

MR. FULLER: Right.

MEMBER SULEIMAN: My comment this morning during my presentation that the uncertainty in radiation organ dose estimation is something that ought to be considered in future medical event criteria, has that registered with the NRC so I don't need to bring that up here again? Did I make myself clear?

MR. FULLER: Yes, it was very clear in the context of the discussion this morning. But I appreciate the comment now because we definitely need to consider uncertainty from a lot of different places, not the least of which is some of the tables that are used and the various tables that are used for the organ dose calculations.

So there is a lot of uncertainty. And you are right, sometimes we kind of focus in on a number as if that is somehow, because we use a single in a lot of these, because the clinicians, the authorized users use a singular number, that somehow we attach to that some sort of certainty. But what we ought to recognize as we develop these rules that there is a lot of uncertainty around those numbers.

MEMBER SULEIMAN: Right. And then I think I stated in previous meetings of the ACMUI that the

precipitin in accuracy of dose estimation using external beam therapy is probably the state of the science. Then you get into seed implants; it gets softer. Then you get into unsealed sources; it is much, much more greater variability.

And so one size doesn't fit all. So that somehow needs to be addressed, taken. Unless it is exam-specific or modality-specific, it could get misinterpreted and run into some of the problems, I think, that we have run into.

That's all.

CHAIR MALMUD: Dr. Welsh?

MEMBER WELSH: Jim Welsh. If I might follow-up on Dr. Suleiman's point. I think it is quite apropos because we tend to think of prostate brachytherapy as being in the same category as external beam in terms of its precision in dosimetry, when in reality for a number of reasons that we have discussed on several occasions, it truly is not. Therefore, using dose for regulatory purposes is going to be challenging.

I don't think that anybody would really want to use dose for radioimmunotherapy. That is self-evident for anybody who is familiar with the modality. But we have misled ourselves into believing that dose

is acceptable for prostate permanent implant brachytherapy and it is truly is not. And I am glad to hear that it was brought up and I hope that the point has not been lost on NRC. I doubt that it has.

But I would like to specifically address your slide number 10 in reference to this particular point. Under key messages, the last bullet point on slide 10 alludes to post-implant imaging should be required. And I like this, despite the fact that I think that there is a typo here. Because my interpretation was that post-implant dosimetry should be required but that wouldn't be consistent with what I have just said.

I think that it is good practice to attempt to do post-implant dosimetry to get some feedback on whether or not if I did an implant, did I hit my targets, my aims as far as giving this approximate dose to this approximate volume. But it would be inappropriate to use this for regulation.

Therefore, the wording might be better post-implant imaging should be required but using that post-implant dosimetry maybe shouldn't be required.

So I am curious about where the imaging versus post-implant dosimetry came from and whether it was intentional --

MR. FULLER: It was.

MEMBER WELSH: -- for this purpose.

MR. FULLER: It was and I will tell you why. This is in the context as if we have a rule that is based upon total source strength or activity, then imaging is more appropriate. Again, there is an assumption here. And as it was explained during the workshops by a number of folks, if we end up with an activity-based rule, it becomes a simple matter of being able to go in and do post-implant imaging and then it is as simple as counting the sources and doing a simple arithmetic calculation to see if you are within the allowable tolerances. So that is why we did the imaging.

Because the dosimetry -- And again if we go to an activity-based rule, a total source strength-based rule, then the imaging becomes something that is outside. In that particular scenario, the dosimetry does become something that is outside the purview of the rules for the target of what we would call the treatment site. I think we are going to probably stick with that term, by the way. It is very generic and we will let folks deal with the others.

But if we are talking about to the treatment site, now I think for unintended tissues and

organs, we are going to have a need to be able to understand what the dose consequences are for things that are not carried out in accordance with the authorized users' intentions. Now I know that we heard it both ways. In one workshop we heard that it was appropriate for us as regulators to maintain a rule. That is why again, I only included the key messages that were loud and clear. So let me be clear on that.

For things that maybe there was a little less consensus or disagreement on, I didn't include those because I wouldn't, at this point in time, consider those key messages. There are things that we heard and things that we will consider.

But we heard in New York that, as regulators, we should maintain the requirements or the criteria for determining a medical event based upon absorbed dose to unintended tissues and organs. Then when we got to Houston we heard just the opposite; that we should not. So we are going to have to look at that again to see what our needs are. But I know when we think in terms of radiation safety, in my way of thinking, the latter. And also in the need to not interfere with the practice of medicine, which is something we take very seriously or study very seriously.

We, I believe, are on stronger footing when we focus on unintended tissues and organs than maybe for the dose or the activity implant or what have you for the treatment site.

CHAIR MALMUD: Thank you.

MEMBER LANGHORST: Sue Langhorst. Going along that line, Mike, we had that discussion in Houston about dose and activity. And I think the important point there is that it all really does come back to dose but you need a metric that people can measure and especially in a somewhat accurate sense, as far as compliance goes.

And so the activity base, even if it is so many percentages of the seeds that are outside the treatment site or whatever term you use, that could be a metric that relates reasonably well with dose, much like NRC uses other types of activity-based regulations that are intended to help meet dose requirements, such as air concentration releases. And that is intended to meet a public dose but it is a concentration because that is an easily measured metric that substitutes for that.

So while you may think you have heard two different things, I think in Houston we were really trying to say what is the metric that you can use that

makes it inspectable and good for showing compliance.

Thank you.

MR. FULLER: Thank you.

CHAIR MALMUD: Other comments? I believe --

MR. CRANE: I have a question from a member of the public.

CHAIR MALMUD: Yes, I believe we have a member of the public who wishes to comment on the subject we are discussing now.

Would you please introduce yourself?

MR. CRANE: Yes, my name is Peter Crane. I am the retired Counsel for Special Projects in the Office of General Counsel.

And my question is for Dr. Welsh. I understand your point about differentiating; the need to differentiate between events that are potentially harmful for patients and that simply involves violation of procedures. Would it solve the problem if each medical event were designated, medical event, paren, potential health consequences, or medical event, paren, no potential health consequences. Would that solve the problem very simply?

MEMBER WELSH: Jim Welsh here. I can respond that conceptually the answer is yes. That if

there were categories that could be of potential medical consequence to a patient, it would be nice to have them so labeled, whether they are in parentheses or given a different term altogether versus those that are simply violations because requirements have not been met. And your categorization might be appropriate.

I am sure there are various permutations on this thing that might solve the problem but the short answer is yes. Conceptually that might solve some of the problems and be better than some of the proposals that we have heard, including my own, of policy violation or regulation requests not met, something of that sort. But the concept is similar and the answer is yes, it might work.

MR. CRANE: Thanks. That's all I have to say.

CHAIR MALMUD: Thank you. And thank you, Dr. Welsh. Other questions? If not, we will move on to the next item on the agenda, thanking Mr. Fuller for his presentation.

And the next item on the agenda is Dr. Welsh, who will present the discussion on the Permanent Implant Brachytherapy Subcommittee discussion.

Dr. Welsh will discuss possible changes to the Subcommittee report. It is agenda item number 17 in your book.

MEMBER WELSH: Thank you, Dr. Malmud.

The first thing I would like to say before going into the conversation in-depth is that I might disappoint folks if they were expecting major changes or possible changes to our prior recommendations.

So if that was what you were expecting because of what was in the handout, I apologize. And I will say that for the most part we are going to stick with our prior recommendation. And the reasons are evident on this first slide.

We are down membership in our Subcommittee. Some of our Subcommittee Members unfortunately have left the ACMUI and therefore their input is not available. And so yes it is a fact that our current recommendations might be potentially different from our prior recommendations. I will refrain from introducing any significant changes for fear of NRC misinterpreting this as ACMUI wavering. ACMUI is not wavering. ACMUI just has different constituency in its Subcommittee. And therefore, the opinions that will be discussed in our conversation and discussion today could be slightly different from

what you have heard in the past. But it is perhaps more due to the change in the makeup than in changing attitudes and general recommendations.

I am going to start by reviewing some of the prior medical events in 2010 that involve 75 patients, 26 medical events, and the majority of these were permanent prostate implant brachytherapy involving 69 of the 75 patients. Some of these were overdoses and they are described here as excess dose to normal tissue, incorrect seed activity, and one overdose that was importantly retracted, based on repeat post-implant dosimetry, which underscores the fact that post-implant dosimetry is not an exact science.

However, the rest of these were underdoses. And this seems to be a general theme that we have seen over and over again and is a function of the current medical event definition. Importantly, two of these underdoses were subsequently retracted and not felt to be genuine medical events because the prostate swelled and, therefore, the volume was different and the dose calculation was altered. And the final reevaluated dose calculation turned out to be within 20 percent and, therefore, this was not considered a medical event. Again, underscoring the

fact that our post-implant dosimetry is not an exact science.

Unfortunately for some of us who have gone on record saying that this could never happen, there was a very unusual event in this time period that has subsequently been retracted because of the definition. In this particular case, the D90 was less than one percent. And I am sure that anybody who has ever performed prostate brachytherapy, who does this regularly, would agree that in this highly unusual circumstance, something has gone awry.

Nonetheless, this particular event was not regarded a medical event because 39 of the 41 seeds implanted were within the target but they were all implanted within a few millimeters of each other on the so-called isoline. And according to the licensee report, the seeds "could have been placed in better location." And I am sure that everybody would agree that that is true. It was attributed to poor image quality but there is probably more to it than that.

Having said that, this unusual event again underscores the inadequacy of the current medical event definition because I think most of us would concur that this probably should be classified as a medical event. According to definitions it might

escape the definition.

The majority of these medical events were based on dose, D90 for the most part. And the question, of course, is would these be categorized as medical events if a different definition were used.

And an important prediction was made a year or so ago that since many of these events that were reported in this reporting period actually occurred in prior years, the prediction was that many more would be expected in future years. And we learned today from Dr. Howe's presentation that that is indeed a prediction that has come true. And it is due to states retrospectively reviewing their permanent implant brachytherapy series and picking up cases that might have been acceptable but meet the definition of medical event.

So the Subcommittee reaffirms its belief that activity-based metrics for the definition of medical event remains preferable. And our prior recommendation that the NRC seek specific help from stakeholders, we are happy to see that that advice has heeded and these workshops have been carried out.

Most Members of the Subcommittee felt that the term "medical event" should be of potential medical significance. And the definition should be

sensitive enough to detect potential harm to a patient. And harm, in most people's opinion, would be direct harm from radiation itself. However, we understand, and for the most part agree, that the NRC is also attempting to identify trends and patterns that could lead to patient harm but not necessarily are overdoses that cause harm to a patient directly and underdoses might fit into this particular category.

And we have heard from Mike Fuller today that whatever it is called, should we come up with different categorizations. We have heard from a member of the public, Mr. Crane, that maybe "medical event" parenthesis this or parenthesis that would be appropriate terminologies. But whatever it is called is less important than what is done with it.

And for the most part, I agree with that. However, I think we also have to be sensitive to what patients -- how patients might interpret that and legal repercussions of the terminology selected might have.

Another key point of the ACMUI Subcommittee report is that post-implant dosimetry is important and should be performed. We learned, much to everybody's pleasure, that NRC has been listening to

us carefully during the workshops and this bullet point probably should be amended to say post-implant imaging is important and should be performed. And I'm glad to see that the workshops are not falling on deaf ears. NRC is listening and is actually a step ahead of ACMUI in this particular bullet point.

However, is post-implant imaging or dosimetry is required, a timeline because a controversial point. Certainly patient-related factors, such as a patient who can't make it or decides not to come in, that should not qualify as a medical event.

How about a slight delay beyond the 60-day proposed limit? Should that be a medical event? Well what if it is 61 days? Is that a medical event? I would say that this is another example of where the term "medical event" might not be the correct word, terminology for such an occurrence and maybe policy violation or something else would be acceptable here.

I understand that if we say that a timeline -- post-implant imaging is important and should be done, you can't divorce that from some type of timeline.

For example, if we are going to say that it is mandatory, what if it is not done within two

years and the inspectors come and the licensee just says well we do ours for two years and one day? We were going to do it tomorrow. Well, that is an obvious and maybe ridiculous example but it is an example of why a timeline is important.

If a timeline is to be imposed, perhaps 60 days should be extended to 90 days. Again, for medical purposes, post-implant dosimetry probably should be done earlier. But for regulatory purposes, if there is going to be a timeline at all, it probably should be more lenient than stringent.

The Subcommittee has suggested in the past that two categories of permanent implant brachytherapy be created. Number one, those which can result in significant rearrangement of the implant location during completion of the surgical implant procedure, such as mesh brachytherapy for lung implants and category two, those procedures that do not have such rearrangements normally. And prostate implants would fall to this category.

Not all stakeholders agree with this recommendation and not everybody on the Subcommittee concurred that this division of categories is appropriate or necessary. I think at this point we do acknowledge that if an acceptable medical event

definition is created, the need for such distinctions goes away.

Here is -- This slide refers to some of the language that still exists and is a holdover perhaps from bygone eras that might no longer be appropriate for this particular modality. In particular, the 0.5 sievert is a very small amount compared to the doses that are being prescribed, much less than one percent.

Number two, a 50 percent overdose might be very medically inconsequential if the original expected dose to that tissue was very low.

And another point that was brought up by a former Subcommittee Member was that the units are inconsistent and confusing and it is suggested that the final rule use appropriate units in a consistent manner or maybe drop this section altogether would be the best solution.

ACMUI has brought this up in the past and, therefore, we felt that it is appropriate to again present these slides. But for the most part, if NRC is in agreement with the activity or source-based definitions, that these alternatives are not necessary.

And I think that this is an important to

time, this is an appropriate time for us to request some feedback from NRC about whether or not our voice is truly being heard. It would seem ample evidence that it is, for example, the post-implant dosimetry being changed to post-implant imaging is a reflection of the fact that NRC is listening. But if NRC is truly listening and moving in the direction of an activity-based definition, our proposed alternative is superfluous.

In the absence of direct feedback to date, the alternative that someone at the Subcommittee has bandied about as suggested is that for the target, D90 less than 70 percent of the CTV and importantly, this is a Boolean and, a dose of less than five percent of the sources occupying any octant of the PTV, except by intent, and specified in the written directive. So those would be the alternative definitions for the target and for the normal tissue, bladder and rectum D5 on post-implant dosimetry exceeding 150 percent of the prescribed dose. Or for the urethra, D5 exceeding 150 percent of its value on the planned, approved dose distribution.

The definition has some attractive features, including the fact that it would catch an event such as the one that occurred last year where

all of the seeds were bunched together. And it would not signify as a medical event an implant where sources are intentionally missing an octant, provided that the overall dose coverage is above 70 percent.

I will conclude by pointing out some statistics on the overall safety of this procedure and the prevalence of this procedure.

First of all, in the years that I have been alluding to in the past, in 2010, 20,000 procedures and only 69 medical events, which amounts to 0.33 percent medical event rate. It looks like it is quite low. It is quite low. It should be much lower, though, because I think that this low figure exaggerates the hazards of this safe and effective procedure. It is safe but I believe that in part due to the inadequate definition, there have been some consequences to this safe and effective procedure's use.

In 2004, 192,000 prostate cancer treatments were administered in the United States. And of those approximately 42,000 were prostate seed implants, accounting for 22 percent of the total.

If you fast forward to 2009 with all the negative listing and the medical event series that have prompted this discussion, we see that there were

220,000 prostate cancer treatments but only about 17,000 permanent implant brachytherapy procedures. The dramatic drop in absolute numbers and more of dramatic drop in overall percentage.

So, I have said this before but I think it is a reasonable analogy to keep bringing up that in prostate cancer brachytherapy, in prostate cancer treatments we have gone from two-dimensional conformal radiotherapy to 3D conformal radiation therapy to improve the targeting and the conformality of our dose cloud. Then we developed intensity modulated radiation therapy for external gain. Now people are talking about proton beam radiation therapy, which is even more conformal. Ultimately, these techniques are going to be almost good as prostate brachytherapy.

And it may sound facetious but it is important to remember that this is a safe and effective treatment and it does provide the best in overall conformality of our radiation dose distribution. But perhaps in part because of the inadequate definition of medical event, sadly for patients in the United States, this treatment is almost disappearing. And I think that is an unfortunate reality.

I will conclude discussion today by

pointing out a few things that were brought up by Dr. Howe in her 2011 medical events presentation. Twenty-five events involving 81 patients. That's a large number. And I don't think it is because of prostate brachytherapy being more hazardous than the other procedures we do involving radiation, involving byproduct material. This is an artificially elevated number due to the fact that some states have been retrospectively reviewing their records and, importantly, not all of these occurred in 2011, which tells us that the ACMUI prediction that if you went back and reviewed very strictly prostate brachytherapy procedures and applied the definition, you might find disappointing results. And these disappointing results are being found.

We have seen that some of these medical events were due to edema, volume changes, or that there was no definite reason for the underdosage, or that there was poor image quality. Underdoses in these situations probably would not be medical events if a proper definition were used.

Another medical event reported that we have heard about today is due to anatomical issues. And if the written directive could be amended prior to completion of the procedure however we define that,

whether it is when the patient leaves the recovery room, leaves the care of the authorized user, whatever, if that written directive could be amended, something like this where the authorized user was a hero and prevented unnecessary harm to the patient, this would certainly not be categorized as a medical event. But with the current definition and regulations, it is called a medical event and I think that is unfortunate.

So it underscores the fact that we do need to change the definition. And coming up with the appropriate definition is critically important because you don't want to see the treatment that provides the best conformality in radiation dose distribution become unavailable to our patients.

VICE CHAIR THOMADSEN: Thank you very much, Dr. Welsh. Comments from the committee?

MEMBER ZANZONICO: I just have a question. You mentioned the timing of the post-treatment imaging and that being as long as 60 days or perhaps somewhat longer if the treatment might be or could be legitimate.

And my question is -- I would have thought that the purpose of the post-treatment imaging would be to verify the placement of the seeds, and perhaps

unsaid, the possibility of implanting additional seeds at some point to correct underdosing and so forth. If that is the case, would it be more logical for the imaging to be done early rather than later or is there some other rationale for the post-treatment imaging?

MEMBER WELSH: Jim Welsh. You are correct that those are some of the purposes for which we would like to do post-implant dosimetry and imaging. And you are correct that if we want to make some changes, the sooner we know that information the better.

But there are some realities. One is that prostate cancer treatment rarely is something that demands urgency. So while there might be an ideal time and an optimal time to do post-implant dosimetry for the purposes of clinical trial reporting or maybe for determining whether or not an additional treatment is necessary, that timeline should be separate from the timeline for which regulatory consequences are to be imposed. And that is why I recommend that for regulatory purposes, if NRC is going to impose such a timeline, that the timeline be lenient rather than stricter.

But you are correct. From a clinical perspective and what are we going to do, maybe sooner is more logical.

VICE CHAIR THOMADSEN: Yes, Ms. Weil?

MEMBER WEIL: I am having a little trouble parsing out this timeline for post-implant imaging. If the clinical purpose for post-implant imaging is driven by better treatment, better outcomes for the patients, then wouldn't the regulatory requirement be driven by exactly the same imperative? Why would the regulatory timeline need to be different if we are trying to regulate good care?

MEMBER WELSH: Jim Welsh again. I think that is a very good question. But I can answer by saying that post-implant dosimetry in an ideal world would give us truly accurate feedback on that particular procedure.

But in the real world, unfortunately, we don't have that degree of accuracy and confidence that the post-implant dosimetry is truly going to give us something that reflects reality. Because as we discussed on many occasions, there are caveats to the post-implant dosimetry, such as the edema and atrophy that routinely occur following prostate brachytherapy and the impact that has on volume. And since dose is energy per unit volume, your dose is going to be slightly inaccurate for that reason alone. And there are numerous other variables such as inter-observer

depth variations. There are modality differences; ultrasound versus CT that further introduce inaccuracies in the dose estimation.

So while we would like feedback and we get that feedback from things like the D90 to learn more about prostate and brachytherapy in general and report this in the medical literature and conduct clinical trials, or we learn on our own as clinicians who perform this procedure and get feedback on am I getting better with time, am I getting worse with time using this particular parameter, we have to acknowledge that the parameter is not perfect and is probably not valid for regulatory purposes.

Getting back to your particular point about the timeline, if the post-implant dosimetry procedure itself has inaccuracies imposing a specific timeline would perhaps not be the best thing for a regulatory purpose.

MEMBER WEIL: This is Laura Weil. But I was specifically talking about imaging. Does that give you a different -- It gives you different information, clearly, than dosimetry.

MEMBER WELSH: You are correct. This is Jim Welsh.

The imaging could be fluoroscopic imaging.

It could be CT imaging. It could be any host of appropriate modalities to image. And I would personally recommend that any practitioner of prostate brachytherapy do post-implant dosimetry but I would not recommend that NRC impose rules and restrictions and punishments if post-implant dosimetry is not performed.

Imaging on the other hand, can be done early using fluoroscopy and a simple seed count and an estimate of how many seeds are in the target but it is probably better done with a more anatomical imaging modality such as CT. And I think that the more lenient time frame is probably better for this purpose.

VICE CHAIR THOMADSEN: If I may, sort of in answer to your question -- This is Bruce Thomadsen. There is sort of a dichotomy right now in that an early image would allow you to make corrections and additions to, well not subtractions, obviously, but additions to, parts of the prostate that may appear to be undertreated. Whereas, the dosimetry done immediately is not very indicative of what the dosimetry should be for the prostate. That comes later. Although later is harder to go back and fix something that you didn't do. Particularly doing two studies is not practical right now because of

reimbursement, which will reimburse one of those studies.

And so the question is, what is somebody going to do? And if they right now have to show that the dosimetry was within the 80 percent, then they are better off doing the image later, when the dosimetry is going to be more like it was at the time of the procedure.

VICE CHAIR THOMADSEN: Other comments from the committee? Yes.

MEMBER WEIL: One more general comment. This is Laura Weil. The title Dr. Welsh for your presentation is permanent implant brachytherapy. But this is specific to prostate.

MEMBER WELSH: Jim Welsh. It is not intended to be specific to prostate. It is intended to be a general request for a medical event definition that is appropriate for all categories of permanent implant brachytherapy.

Because of the challenges and the significant differences between prostate brachytherapy and the others, we have suggested that maybe there be two separate categories. Basically, prostate and non-prostate or procedures in which there is a rearrangement and not rearrangement. But if we could

come up with an appropriate medical definition, it should and would encompass everything in permanent implant manual brachytherapy. And that is our ultimate goal, to seek a definition that would be appropriate for all of them. If we cannot, then maybe having subcategories is a better idea.

But our initial charge was to address the entire category of permanent implant brachytherapy but the reality was that during the time frame that prompted all of this in the first place, the majority of medical events were prostate brachytherapy, the overwhelming majority, and the negative publicity in the press was focusing on the prostate seed brachytherapy problems.

And so it looks that the majority of our discussion is focusing on prostate brachytherapy for those reasons.

VICE CHAIR THOMADSEN: Yes, Mr. Einberg?

MR. EINBERG: Chris Einberg here. Dr. Welsh, is it safe to assume then that your Subcommittee report does not have any changes to it? And the reason I ask that is that we are -- the NRC Staff needs to provide ACMUI its views on prostate brachytherapy implants or definition of medical events to the Commission.

And so has the report changed? Or if not, can the Committee re-endorse the Subcommittee report?

MEMBER WELSH: Jim Welsh. I am going to ask for input from the remaining Subcommittee Members as to whether or not there is consensus on whether or not there needs to be any changes.

My general feeling is that we don't have to make very many changes but I am just one of three people.

VICE CHAIR THOMADSEN: I think you are asking two very different questions. And one is whether the Subcommittee's report has changed, to which Dr. Welsh has pointed out his reasons why maybe not, only because the Subcommittee is not what it was.

And the other is, what is the ACMUI's position on this. I think that the ACMUI is going to have to make a statement on that.

Yes, Mr. Fuller.

MR. FULLER: This is Mike Fuller. Just to kind of remind folks of one, I think important, point. Last April when we were talking about delaying one of the workshops, it all comes down to schedule. Well not all, but sometimes. When we were talking about moving one of the workshops from June to August, it was with the caveat and the assurance that by this meeting we

would have the ACMUI's view or endorsement or whatever you want to call it of the brachytherapy subcommittee's report. Because as we explained then, we need that to help us meet our schedule. We owe the Commission something in November on this.

So I think that is what has popped in Chris' question. In other words, does it need to be changed further before the ACMUI can take it up or is it good enough for the ACMUI to endorse? So that is really what we are getting at.

VICE CHAIR THOMADSEN: I understand your question and I think that by the end of the meeting we should have the answer. I don't see that that is a conflict at the moment.

Dr. Langhorst, did you, as the other Member of the Subcommittee, have you a comment?

MEMBER LANGHORST: This is Sue Langhorst. I know, given that we have lost two members of our Subcommittee, Dr. Welsh rightly so was concerned about the remainder of us having a little different opinion in changing the Subcommittee report without those other inputs.

And so I think that was one of the questions we were bringing to the Committee today. We felt it was unfair to ask someone to jump in and give

a quick opinion if they were, for instance like Laura Weil, brand new to the Committee.

So I think that is one of the questions we kind of had of the Committee as to whether you think the three of us should go ahead and propose a final Subcommittee report and have the full Committee take that up or would you feel that we need to have a couple of our people's input on where we are with the Subcommittee report and bring it to the full Committee say in the next few weeks or so through a teleconference?

So I think that was kind of the question we had of the full Committee, how you wanted us to proceed, given the change in our membership.

CHAIR MALMUD: This is Malmud. I would assume that the Committee, even absent the two former members, did come up with a recommendation. And the -- let me see if I can explain to you how I see this in my mind and maybe that will help, though it may cloud it as well. I can't predict that.

By way of background, particularly for those who have just joined the Committee, the prostate is like a lemon that sits in the perineum through which a straw runs the urethra. Okay. That's the way it sits. The implantation of seeds in the prostate is

done with the man in the dorsal lobotomy position most often, a grid placed over the perineum, and the seeds put through holes that are perforated in this metal grid.

The implantation is a skill, it is imperfect, and it appears that those institutions that do it frequently do it well, and those institutions that monitor and teach those who do it do it extremely well. However, as soon as a rod containing the seed penetrates the lemon, the lemon begins to swell, and it swells in an irregular fashion, assuming no infection, just the mere penetration of the tissue it swells.

Hence, the geometry changes. Hence, what was imaged before the process is now distorted. It's distorted by the very process itself. And as each seed is implanted, the distortion increases due to the physiologic swelling in response to the prostate being penetrated.

The seeds can sometimes go into the urethra and sometimes go into the adjacent organs, the bladder or the rectum, where the lemon is sitting ensconced.

The experts in this area -- and I am not one of them, so I'm describing -- this is as someone

who doesn't do this procedure but has only been educated by the members of this Committee. The process results in, when done well and when it reaches the clinician's goal, is a very effective therapy in treating prostate cancer.

The complications are obviously those of the implantation of the seeds, and that can be irradiation to excess of the bladder, the rectum, and also grouping the seeds too much in one part of the lemon, leaving the other portion of the lemon, which may contain some tumor, untreated. And these are all possibilities in the hands of even the best therapists.

When things go awry, when too many of these seeds -- and there is no firm definition for the number, what that number is as a percentage of the total -- go into the wrong area or are concentrated in one area, the physician, from the medical perspective, is disappointed in the result, and the patient may be disappointed in the result as well.

So what we are dealing with is a technique which is a skill and for which there is no guarantee. Now, add to that the following, the imaging has been done in the past by ultrasound, and more currently by CT. But it isn't done by CT in every institution

currently. And please stop me when I make an error, Dr. Welsh. It doesn't done by every institution currently. Some still use ultrasound.

Some have not even done post-therapy imaging for a variety of reasons -- perhaps downtime in their equipment, patient non-compliance. There may be a number of issues, and, therefore, there is no attempt to estimate the results of the therapy by imaging and by calculations of doses, except for the theoretical that was done pre-therapy.

So what we are looking at, from the NRC's perspective, is not the practice of medicine, which is not technically our responsibility -- it's not the mission of the NRC -- but the radiation hazards associated with this and to look at incidents in which radiation outcomes result in untoward effects to the patients.

We have been careful not to intrude into the practice of medicine. Now, as an observer, as a non-radiation oncologist, it seems to me that at this point in history that the specialty group that governs radiation oncology should require of its practitioners that they do post-implantation imaging. And I'm using the term "imaging," not "dosimetry."

From the imaging, a skilled radiation

oncologist will estimate the radiation burdens to the various parts of the organ that were intended to be treated, as well as to adjacent organs that were not the goal, the target.

It is like pornography, defined by the Supreme Court, "when you see it, you know it." But it's very difficult to define. And this is a skill; this is an art form, for lack of a better term.

And to judge severely a treatment that has gone awry may be unjust, in that the treatment may have gone awry for purposes which are -- have nothing to do with the skill or the goal or the patients with which the procedure was performed.

We, in the NRC ACMUI, are concerned about the severe untoward effects that could have been prevented. And what can we do in the future about preventing them? And this has been an ongoing struggle for all of us, and it seems to me that if the governing board for the radiation oncologists don't demand that there be at least post-therapy imaging, assuming patient compliance, that it may be our responsibility to recommend that it must be done, so that at least there is a record, if necessary, some documentation of whether or not something really was done improperly.

My understanding, though, as an outsider again, is that not all the institutions that perform this procedure have CT available to them all the time. And I don't know whether it is the state of the art currently, but that could be demanded or that would cause some institutions which provide this therapy to stop providing the therapy, which itself would be perhaps an unhappy event for the members of the public who need treatment.

But it is very difficult to measure the unknown with the unknown. It is very difficult to judge the unknown with the unknown. And at least if we had post-therapy imaging, we would know where to begin in the event that an investigation were necessary. But I wouldn't -- I would be hesitant to charge someone with having done less than optimal therapy if it turns out that the seeds were not exactly where they were wanted in a percentage or some percentage above what the goal was.

Let's say the goal was to get 80 percent to the target, if that particular patient had an unusual amount of swelling -- and I'm not even discussing the fact that infection, if present, would even distort the lemon further. I don't think we have the data. Despite the volume of cases, I don't think

we have the data that we need to make a recommendation other than the recommendation that we have made, which I concur with, which I personally concur with.

But I would like to see the specialty board, if not us, demand that the protocol include post-therapy imaging. Not necessarily the calculation of the dose, if the dose calculation is going to get them into trouble, but at least demand the post-therapy imaging.

Dr. Welsh, your response, please.

MEMBER WELSH: A quick response to this important point is that the professional societies have uniformly endorsed post-implant dosimetry or post-implant imaging. And the reality is that our professional societies are not regulators, and, therefore, although it is strongly recommended the recommendations of ASTRO, American Brachytherapy Society, other professional societies, are recommendations and not absolute requirements. And somebody who fails to comply with these recommendations is not in violation of any particular law.

Now, having said that, it would at this point fall outside the standard of care in 2011, 2012, for any practitioner or institution that routinely

1 does prostate brachytherapy to not routinely comply
2 with the professional society recommendations. So if
3 they are not complying with those recommendations,
4 they should not be doing the prostate brachytherapy.
5 CHAIR MALMUD: It's my understanding, in
6 response to your statement, that if that's the
7 recommendation of the professional societies, and
8 those recommendations are not being met, that there is
9 no penalty that can be imposed by the professional
10 societies except that the credentialing committees of
11 the individual hospitals could reject it. But if it's
12 done in a freestanding regular therapy unit, there is
13 no similar body.
14 So does it then become our responsibility
15 in protecting the public to dare to enter the realm of
16 requirements? We do that in some areas. We do that in
17 requiring dose calibrators for regular
18 pharmaceuticals. We do that in radiation oncology's
19 groups. We are thinking of the best interests of the
20 patient, and also in not preventing the patient from
21 getting a modality at the same time.
22 MEMBER WELSH: This is Jim Welsh. It's a
23 difficult question to answer, because there is a very
24 fine line between intruding into the practice of
25 medicine here. Nonetheless, there is nothing that our

professional societies can do that is legally enforceable, and, therefore, if we were trying to come up with some way of saying, "How can we make sure that post-implant imaging is truly being performed?" it's not going to come from a professional society's recommendation.

It could only come from a regulator's insistence, which, again, is a very fine line. And it could intrude into the practice of medicine, and it could further exaggerate these already alarming figures that show a decrease in the prevalence of this treatment.

But it is important to follow up with another point regarding your lemon analogy. And, yes, this is a procedure that is fraught with some technical challenges. There is an art to it. There is definitely a skill to this. There are a number of areas that things can go awry.

But having said that, it is important to remember that the published literature supports the fact that of the available modalities for early stage prostate cancer, this may be the best in terms of its effectiveness and side effect profile when viewed together. And it compares very nicely with the gold standard of surgery, including the modern robotic

surgical procedures, and with external beam radiation therapy, which has improved immensely over the past decade. This prostate brachytherapy remains a very --

CHAIR MALMUD: I didn't choose the lemon as a piece of fruit to judge the --

(Laughter.)

Perhaps I should substitute kiwi for lemon to make it more acceptable. I was trying to reach the size of the organ that is being treated approximately. I thought an orange or a grapefruit would be excessive.

MEMBER WELSH: Nonetheless, the lemon might be better than the kiwi, because trying to penetrate that capsule can cause the needle to bend in a direction that you don't expect or don't want it to bend, introducing further need for skill and experience on the part of the user.

And in the hands of an experienced prostate brachytherapist, this treatment is very effective and very safe.

CHAIR MALMUD: Dr. Thomadsen.

VICE CHAIR THOMADSEN: I would guess that requiring post-procedure imaging would not be one of the factors that would be reducing the number of cases being done, and that that sort of has been the

standard practice for a long time now. And I'm not sure that that would really reduce the number of opportunities for patients to receive this care.

In the past, people have done it because they have had to show that the dosimetry is within the 80 percent as in the guidelines by the regulations. If they now just have to show that the number of seeds are correct, I don't think that that would affect or reduce the number of cases that would get done.

CHAIR MALMUD: If I may, the reason that I brought up that suggestion was because of the notoriety surrounding the last major instance at the Philadelphia VA in which there was no imaging done. Had imaging been done -- and I'm not privy to all the details with the case, but had imaging been done earlier they would have recognized that they were going astray long before they did, even without calculating the precise dosimetry.

Am I correct in that assumption, Dr. Welsh?

MEMBER WELSH: I believe that you are, and I believe that if there were a series of patients who did not have post-implant dosimetry for a variety of reasons, including I believe problems with the operation of the equipment technically and making it

unavailable for a while, if the institution was routinely insisting on performing as recommended by professional society standards, and doing the post-implant dosimetry regularly, that it probably would have curtailed the number of reported events.

CHAIR MALMUD: Dr. Suleiman.

MEMBER SULEIMAN: Conceptually, stepping back, the way I see things is that it works into the culture. You know, the societies advocate, adopt, recommend certain things like imaging or whatever. And at that point, hopefully, the vast majority of practitioners are doing -- are behaving that way.

And if that becomes accepted practice in standard of care and problems occur because people are deviating from that now accepted standard of care, I think it's at that point that maybe it becomes a regulation to ensure that people are doing things properly.

I think for a regulator to step in before it has been established as a standard of care is presumptuous and can cause problems. So I think the natural progression of voluntary standards, and then, at some point -- if there is a safety issue. So I don't see anything wrong in this progress.

MEMBER WELSH: Jim Welsh. I would reply

that I concur that the society recommendations, the policies that have been set forth, the guidelines that have been published and recommended, do demonstrate that this is standard of care. And it has been standard of care since this was published over a decade ago. And, therefore, it is perhaps not unreasonable for a regulator to step in now to make sure that the standard of care is being adhered to.

In general, I don't like the idea of the regulators coming in and imposing this because of the possibility that it is encroaching on the practice of medicine. But your point is well taken that there is a sequence, and the sequence is that this is the established standard of care, and those who have not been adhering to it have caused a lot of ruckus and problems for all parties involved, including the regulators, to the point that it is probably appropriate that the regulators could step in and insist on this.

CHAIR MALMUD: Dr. Thomadsen?

VICE CHAIR THOMADSEN: In addition, no matter what definition ends up being selected for the event criteria, in order to evaluate it will require imaging. Otherwise, there will be no way to know if the criteria are met.

CHAIR MALMUD: That's a valid statement. Dr. Langhorst?

MEMBER LANGHORST: Getting back to the Subcommittee's report, I do think that there are a few what I'll call tweaks that we probably would like to make to the report. An example would be about using the current nomenclature of -- oh, gosh, help me with that.

MEMBER WELSH: GTB, CTB.

MEMBER LANGHORST: Right. That maybe we don't agree with that recommendation anymore, that we like the term of treatment site, given its generic use, that that doesn't require regulations to be that prescriptive. And I guess the question is, is whether the Committee would be comfortable with the three remaining Subcommittee members making those few tweaks and providing that updated report to the Committee for approval.

CHAIR MALMUD: For the record, would you indicate the specialties of the two members who have left the Subcommittee?

VICE CHAIR THOMADSEN: One is a radiation oncologist, and who is the other one? Oh, yes, the other is the state representative.

MEMBER WELSH: I think there was a third,

then. The patient advocate.

MEMBER LANGHORST: Patient's advocate. We had five members of this most current report, and that was Debbie Dilley, Dr. Fisher, myself, Dr. Thomadsen, and Dr. Welsh. So it was our patient advocate and our state -- Agreement State representative.

CHAIR MALMUD: We currently have no Agreement State representative, but could we add back to the Committee, if it could -- if the Subcommittee would accept it, the new patient advocate and then let that Subcommittee make its final report? Dr. Welsh.

MEMBER WELSH: If I might request or suggest that Dr. Thomadsen's point about the radiation oncologist leaving is not in error. It is that when we were first starting this, we had Dr. Nag as a member of our ACMUI. But before the Subcommittee could get fully operational, Dr. Nag's term expired, and there was a long interval in which there was no other radiation oncologists that were -- it sure seemed long to me.

Now that we do have another radiation oncologist, in that we had -- and this is a radiation oncology issue, I'm wondering if our other radiation oncology member on the ACMUI would be better -- would be an ideal additional member.

CHAIR MALMUD: Dr. Suh?

MEMBER SUH: Let me just share my thoughts. So prostate cancer is obviously a very common malignancy among men. It's a very important cancer that we have a number of treatment options for. Prostate brachytherapy has been clearly shown that, in the right hands, it is a very effective treatment option for patients.

It is unfortunate with the events that occurred in Philadelphia VA that a lot of attention and scrutiny have been pointed towards the prostate brachytherapy procedure, which has been shown for many years to be an effective treatment.

The current definition is a source of concern from not only myself, but also several societies as well, because the current definition is -- makes some implants be perceived as a medical event when probably in all actuality it is probably not a medical event.

I support the idea in terms of the Subcommittee. I have been here for about a year now. In terms of using an activity-based metric, that makes more sense than a dose-based metric for all the things that you mentioned earlier, and others here have mentioned as well.

I think it is important that we have post-implant dosimetry, because if you don't know what you have implanted, you will never have an idea of whether or not you have done a good or perhaps a suboptimal implant.

So in terms of Dr. Welsh's volunteering me to be part of the Committee, I would be happy to do that if that would be valuable to the rest of the members.

CHAIR MALMUD: The Committee would be very pleased if you would do that.

MEMBER GUIBERTEAU: Could I ask -- John, could I ask a question? When you say that post-implant dosimetry should be part of the procedure, do you mean it should be required?

MEMBER SUH: Well, it's something that, again, I would like to discuss with the other Committee members.

MEMBER GUIBERTEAU: All right. That's fair. But -- so you haven't reached that decision at --

MEMBER SUH: I think imaging -- imaging is important, and I think that it's something I would like to get a better handle on from the Subcommittee as well.

MEMBER GUIBERTEAU: But if I could just add, it's confusing to some of us who don't do this that I think the Committee needs to come back with a recommendation, when you say "it should" or "it's recommended." I mean, either, you know, this Committee in terms of being -- in terms of the safety and regulation of what is being done, I mean, we either are requiring it or we're not.

And, you know, we are not really in a position to recommend it, because that is really the practice of medicine, and people should be doing that. So I would ask personally, just for my benefit, to come back with some clear wording as to what we are doing with post-implant imaging.

CHAIR MALMUD: Dr. Welsh?

MEMBER WELSH: I would respond to Dr. Guiberteau by saying that -- absolutely right. And our Subcommittee report has alluded to this, but I like what I heard today from Mr. Fuller in his slide number 10 saying that post-implant imaging should be required.

I think that states it very succinctly, and I think that the Subcommittee in general, and the ACMUI as a whole, probably endorses that statement and likes it better than post-implant dosimetry should be

required, because it then doesn't impose on the practice of medicine nearly as much, and --

MEMBER GUIBERTEAU: Thank you.

CHAIR MALMUD: I presented it as a step. I didn't want to intrude on the practice of radiation oncology, and ACOG already has recommended it. So we're not really -- we're not really endorsing anything that has been opposed by the professional society.

Dr. Suleiman?

MEMBER SULEIMAN: I think, really, it's an issue of verifying somehow. And I think dosimetry is used pretty loosely, and I think you can't do the -- you can't do good dosimetry in this situation without some imaging. So I think imaging, to me, seems more logical. And the proof of the pudding, to me, would be, without the imaging, is there a safety issue?

You know, are there populations out there that hadn't done the imaging and clearly there is a greater risk to those patients? And I think if that answer could be yes, then it is a step to adopting what -- good practices in a more mandatory way.

CHAIR MALMUD: Dr. Welsh?

MEMBER WELSH: I will respond by saying Dr. Thomadsen's point is important, that you can't apply

this proposed definition without imaging. And so imaging is an inherent component of the definition. It is perhaps reasonable to explicitly state that imaging is necessary and should be required. But post-implant dosimetry is a subset.

And although the professional societies and I personally think that we should all be doing post-implant dosimetry, it, in my opinion, might be best kept out of the regulatory realm, because post-implant dosimetry leads to a dose calculation which takes it down the wrong path.

CHAIR MALMUD: Dr. Langhorst?

MEMBER LANGHORST: Thank you. I just want to remind the Subcommittee, and also the Committee, to be mindful of NRC's request of timeliness of this revision and then review by the Committee. And so I think we need to be mindful that we need to do this on a fast track to hopefully help support that effort. So --

CHAIR MALMUD: Thank you for reminding us of that. Are the members of the Subcommittee prepared to do that in a reasonable --

MEMBER LANGHORST: I am.

CHAIR MALMUD: You are. Dr. Welsh?

MEMBER WELSH: Yes.

CHAIR MALMUD: Dr. Suh?

MEMBER SUH: Yes.

CHAIR MALMUD: This may be late for you to join in on this, given the fund of knowledge here has taken several years to accrue. All right. So then, Dr. Thomadsen, you are going to join the group as well?

VICE CHAIR THOMADSEN: Absolutely. Would you like to propose a deadline for the Subcommittee's report?

CHAIR MALMUD: I would like to hear the chair of the Subcommittee propose a deadline aggressively, so that we can endorse it.

MEMBER WELSH: This is Jim Welsh. In order -- before I can propose a definite deadline, could somebody repeat the deadlines that are necessary for the Commission, so we have a good idea again?

CHAIR MALMUD: Mr. Fuller? The deadline that you would like to see met?

MR. FULLER: According to our current schedule, we owe the Commission what we call a CA note with this Subcommittee's report attached by November 4th. So it's very -- and, of course, Neelam can keep me honest, but that's the right date, correct?

MS. BHALLA: That's correct.

MR. FULLER: Okay. So --

VICE CHAIR THOMADSEN: Can I ask, Mr. Fuller, in order for you to do that, how soon do you need to have the Committee's decision?

MR. FULLER: Ashley has her hand up. I think -- did I misspeak, Ashley?

MS. COCKERHAM: No, you didn't misspeak. But I think we also have a SECY paper that needs to be drafted that also includes this that's due -- is that -- that's due in -- I can't remember the date.

CHAIR MALMUD: October?

MS. COCKERHAM: We need this in mid to early October, if possible. Does that answer the question?

MR. FULLER: Yes, I -- we were just talking about that normally, you know, for us to get something -- after we have received it, to get it through concurrence, and so forth, we look at 10 days or two weeks, but we could try to -- we could try to really fast track it ourselves. In other words, you know, run it around and brief various people.

So it -- Ashley has her hand up again. She is going to keep us straight again.

CHAIR MALMUD: Ashley?

MS. COCKERHAM: A light bulb came on. We have a SECY paper due in March. If you back up all the timelines, the October date still stands. It takes a month or more to get a paper through concurrence. The paper has to be drafted, and our SECY paper actually cannot be drafted until this report is submitted and final and included in it.

It is the basis, if you will, of our paper. We have to provide the ACMUI position and the staff position. So I'm not sure about this CA note. That's not ringing a bell right now. But the SECY paper is due in March, so the October -- mid to early October date still stands for this Committee report to be final, voted on by the Committee in a public meeting.

MR. FULLER: Yes, I would -- what I would like to ask for, if at all possible, I know that November 4th date is on a Friday. So the previous Friday I think is October 26th, is that correct?

MR. LUEHMAN: 28th.

MR. FULLER: 28th? So, I mean, at the very latest, if we had something that had the endorsement of the full ACMUI by October 28th, then we would have -- I know I'm really, really being aggressive, but I want to give folks the -- you know, the --

MS. COCKERHAM: No, you're not being aggressive enough.

MR. EINBERG: Chris Einberg here. That won't work.

MS. COCKERHAM: The CA note I believe that you're thinking about is for ACMUI-ACRS best practices, which was from my pro-con SECY paper. That's the CA note that we owe in -- but for --

MR. FULLER: I know Neelam is getting ready to make a presentation about the schedule, so it will become more clear after that. I'm sorry, I just don't have the dates in front of me.

MR. EINBERG: Neelam, can you come to the microphone, please?

MS. COCKERHAM: I'm going to say -- sticking by early to mid October.

MS. BHALLA: This is Neelam Bhalla from NRC. What our CA note to the Commission is looking for -- and actually that's going to be in my presentation, but I'll address it right now -- the Commission asked us that after the workshops give a note to the Commission that the status -- as to when can we do this rulemaking and give them a schedule.

So it's a chance for us to go back to the Commission and say, you know, these are the issues,

and we think this is the guideline. We have already provided a timeline to the Commission in an IP paper, that SECY-11-0035, and so right now we are planning and we are hoping that we will stay with that schedule.

But the Commission note -- the CA note in November will be to let the Commission know if we see any problems, or would we be able to meet the schedule. If not, why not? And also, Commission wants to know what the effect of that schedule would be on the larger medical community.

So we do owe a note to the Commission in November. The exact date is -- you know, whatever that date is for us that becomes two weeks prior to that date because of the way our members move up to the Commission.

So to go back to what this Commission note is about, the schedule, and basically we will be giving to the Commission that, yes, we can meet the schedule that we have right now. But one of the basics in that report that went out, that for the medical event we are counting on the ACMUI report, because that becomes the basis or the starting point for the technical basis for this medical event definition. And if we don't have that report on time, it is going

to delay our schedules.

CHAIR MALMUD: Thank you. So we would need a report from the Subcommittee, and then we need a formal meeting of the Committee, which could be a telephone conference call. But that would have to be entered into the Federal Register.

MEMBER LANGHORST: Right.

CHAIR MALMUD: So what is the timeline for entering a telephone conference call into the Federal Register for the ACMUI? How many weeks do we need in advance?

MS. COCKERHAM: We need 15 days.

CHAIR MALMUD: Fifteen days. So if we take 15 days from October 30th, that would bring us back to October 14th or so. Could the Subcommittee have its report ready for the full Committee before October 14th? Last question is addressed to you, Dr. Welsh, and members of your Committee.

MEMBER WELSH: Dr. Thomadsen has -- is signaling to me in sign language.

CHAIR MALMUD: Dr. Thomadsen is signaling October 7th. Is that a possibility for the Subcommittee, October 7th?

MEMBER WELSH: As the chair of the Subcommittee, I can say that since most of what we

will be doing is tweaking rather than rewriting, we should be able to adhere to an October 7th deadline, provided that our new members get copies of the Subcommittee report, the original one that we are about to amend, as soon as possible. And we can start working on this and have it finished very quickly, certainly meeting that deadline.

CHAIR MALMUD: So you think you could get your work done by October 7th, and we could enter the date for the conference call for the entire ACMUI and have it before October 30th? Ashley, you're shaking your head. Not possible?

MS. COCKERHAM: The October 7th date is fine for the Committee report. We can publish a Federal Register notice. We can draft it next week and publish it, you know, late next week or early the week after that, and go ahead and set the date for -- it could be October 8th, the day after your Subcommittee reports. That's a little -- I mean --

MEMBER LANGHORST: That's a Saturday.

MS. COCKERHAM: I am exaggerating. But the telephone conference could go ahead and be noticed now, and the Subcommittee would have until the 7th to do their report and, say, give the Committee a week to review the reports and already have the teleconference

scheduled for October 14th. I don't know what days those are. Are we scheduling dates on Saturdays?

MR. EINBERG: October 14th is a Friday.

MS. COCKERHAM: Okay. Probably not the best date, but does that seem agreeable?

CHAIR MALMUD: October 19th is the following Wednesday. Is that a good date for the conference call?

MEMBER SULEIMAN: I am in the air --

PARTICIPANT: Me, too.

CHAIR MALMUD: What day would be preferable to you?

VICE CHAIR THOMADSEN: Tuesday -- would Tuesday work? Monday or Tuesday, the 17th or 18th, would that work for --

CHAIR MALMUD: Dr. Welsh?

MEMBER WELSH: The 17th or 18th, which are Monday or Tuesday, or the 14th, which is the previous Friday, would work for me.

CHAIR MALMUD: The previous Friday, would that work for you?

VICE CHAIR THOMADSEN: Well, that's --

CHAIR MALMUD: Sue, I think --

MEMBER LANGHORST: Sue Langhorst. This would be for the full Committee.

CHAIR MALMUD: Yes.

MEMBER LANGHORST: So we need -- I can make anything work.

CHAIR MALMUD: Okay.

MS. COCKERHAM: What is the date for consideration again, really quickly?

MEMBER WELSH: We are thinking about the 14th, the 17th, or the 18th. And I guess if anybody has a problem with those that might be a better way --

MS. COCKERHAM: Any time after the 17th would be good.

VICE CHAIR THOMADSEN: After the 17th.

MS. COCKERHAM: After the 17th.

VICE CHAIR THOMADSEN: That sounds like the 18th.

MR. EINBERG: And that's because of the 15-day FACA requirement?

MS. COCKERHAM: Yes.

CHAIR MALMUD: October 18th?

MS. COCKERHAM: Sure.

PARTICIPANT: It's a Thursday?

MS. COCKERHAM: Tuesday.

CHAIR MALMUD: Fine. So be it. October 18th.

VICE CHAIR THOMADSEN: That day I can do

any time, whatever --

CHAIR MALMUD: Dr. Suh, is that good for you? Dr. Welsh?

MEMBER SUH: That's fine.

MEMBER WELSH: Yes.

CHAIR MALMUD: Dr. Langhorst?

MEMBER LANGHORST: I can make anything work on that day.

CHAIR MALMUD: October 18th it is.

MEMBER LANGHORST: For the full Committee, though.

CHAIR MALMUD: I just want to do members of the Committee first. That's why -- I wasn't ignoring you, Bill. One, two, three, four. So the four members of the Subcommittee can make it on October 18th.

Thank you. Dr. Van Decker?

MEMBER VAN DECKER: I just want to ask a question, so I'm not reading too much into this. First of all, I have nothing but the greatest confidence in the remaining Subcommittee members that they have a feel for the field, and that this is working in the right direction, that tweaking this is fine, and we can do all of this.

But I guess this concept of the statement

of we've lost some Subcommittee members makes me just raise this question and think about it.One of those Subcommittee members was the representative of the states, and we just talked about this issue of getting this through, the proposed rule through the states as well. So it's got to come out in some fashion where they feel that they have buy-in to it.

So I guess my question is: as far as you know, Debbie, when she was part of this, was not expressing a strong minority opinion about something that we need to know about, have some sense for, and --

VICE CHAIR THOMADSEN:I had very extensive discussions with Debbie on about three occasions about the proposals. And I think I know what her take on that was as far as the states. And I was at the OAS meeting and heard a bunch from many of the people from the states about the proposals. So I think that -- I think I do have an idea of how the state radiation control people have felt about this.

CHAIR MALMUD: Does that answer your concern, Dr. Van Decker?

MEMBER VAN DECKER: Yes. I just don't want us to set ourselves up for more problems down the line. But this is --

CHAIR MALMUD: Thank you.

MEMBER VAN DECKER: -- where we are, and that's fine. As long as --

CHAIR MALMUD: Mr. Einberg?

MR. EINBERG: Because this meeting will be publicly -- a public teleconference, we could invite or inform the Agreement States to participate and perhaps provide them with an advance copy for their review also to ensure that their views are understood and heard.

CHAIR MALMUD: Thank you. Dr. Welsh, do you have anything else you want to say to us?

MEMBER WELSH: I have said enough.

(Laughter.)

CHAIR MALMUD: Any questions for Dr. Welsh, or comments?

(No response.)

Thank you. It has been a very constructive session. I think that we are all -- all of us here have dual -- oh, I'm sorry.

MEMBER MATTMULLER: Do we need a time for our teleconference for Ashley?

CHAIR MALMUD: Yes. You'll work that out. Ashley, do you have a time? Sophie or --

MS. COCKERHAM: Yes, now is as good as any.

Do you have your calendars or -- yes? I know we have people on the west coast, so nothing before 11:00 a.m. Do we have anyone on the west coast now? No?

VICE CHAIR THOMADSEN: Well, the state people, but --

MS. COCKERHAM: State people, okay. Let's consider -- nothing before 11. Okay. Is 11 good?

MEMBER LANGHORST: Eleven is perfect. This is Sue Langhorst. That's perfect for me.

MS. COCKERHAM: Okay. 11:00 a.m. Eastern Time.

MR. EINBERG: And how long is the meeting?

MS. COCKERHAM: We will probably have --

MEMBER LANGHORST: I was thinking Central Time.

VICE CHAIR THOMADSEN: It's Eastern Time, so what time are you -- 12 is fine.

MS. COCKERHAM: 12?

CHAIR MALMUD: How is 12?

MS. COCKERHAM: Okay. How is 12?

VICE CHAIR THOMADSEN: 12 Eastern Time.

MS. COCKERHAM: 12 Eastern?

MEMBER LANGHORST: yes.

MS. COCKERHAM: Okay.

PARTICIPANT: And this is the --

CHAIR MALMUD: ACMUI teleconference.

PARTICIPANT: And how long did we say?

PARTICIPANT: Approximately two hours or less.

MR. HAGAN: Can I make a comment from the public?

CHAIR MALMUD: Oh, a comment from the public, who is invited. Absolutely. Please introduce yourself.

MR. HAGAN: I'm Mike Hagan. I'm the National Director for the VA for radiation oncology, hired in the wake of Philadelphia brachytherapy issues that you have mentioned several times today.

A comment and a request. The comment is imaging was done in Philadelphia. Imaging is available now in all of those patients, save seven that couldn't be found in archives, but 107 patients. And clearly the imaging was done -- or was not done as any quality assessment.

So no metric at all was applied, not from a clinical standpoint, not from a regulatory standpoint. And so when the VA had to design and then apply a metric to evaluate those cases retrospectively, they opined and then selected an absorbed dose metric.

Absorbed dose metric, as you have heard through the workshops, is very problematic, and you have moved away from that. In fact, you moved away from that in 2005, and now you are, with good confidence and with good support from the professional societies, move away from an absorbed dose metric to an activity metric.

The point that I would make is that an activity or a source strength metric is entirely in keeping with your current language for Part 35. The definition of "dose" for manual brachytherapy has two parts, and one of those parts is activity times time equals dose.

So the application of the 20 percent standard for a source strength based metric fulfills your current regulatory requirement. So I think it would be quite helpful, because several practitioners of national refute have indicated that the confused regulatory environment now has caused them to stop practicing this procedure.

So the idea of perhaps suggesting or requesting NRC to issue guidance that the application of an activity metric for regulatory evaluation is appropriate during the interim period when new language is being proposed may be helpful not only to

the practice but to the issue of reducing some of the regulatory confusion that exists today.

CHAIR MALMUD: Thank you. Dr. Welsh, do you care to address the comment?

MEMBER WELSH: Well, I think Dr. Hagan's input is always appreciated and the point is an important and valid point, an important point that although we are saying that we are shying away from a dose-based metric and this could be a little bit difficult for someone -- NRC to accept or to really endorse.

We are implicitly using dose by the definition of activity times time gives you dose. So I'm -- for the most part, I concur with Dr. Hagan's input.

CHAIR MALMUD: Thank you. And having heard your concern, Dr. Hagan, the Subcommittee will come to a resolution that will incorporate, to the extent possible, your concern.

What I was about to say earlier was that there are a number of therapies available toward treating prostate cancer. This has been a very valuable member of that armamentarium. It has been damaged not by anything that the NRC did, but it has been damaged. And as soon as we can assist in

establishing, with the specialty groups, guidelines which will restore both physician and the public's confidence in the technique, the more rapidly it will resume its important role in the treatment of prostate cancer.

Thank you. We will move on to the next item on the agenda. And I want to thank, again, Dr. Suh, you have -- we have now volunteered you for two Subcommittees, and you have accepted both.

MEMBER SUH: That's right. That's what I'm here for, so --

(Laughter.)

CHAIR MALMUD: We are now up to the Part 35 rulemaking update, and that will be presented by Dr. -- Bhalla and Lohr from the NRC. Ms. Bhalla and Mr. Lohr will provide an update to NRC Part 35 rulemaking activities.

MS. BHALLA: Good afternoon, Dr. Malmud and members of the ACMUI, and, of course, the members of the public. This -- we are going to give a very, very quick update basically on the status of the expanded rulemaking Part 35.

I am Neelam Bhalla. This is Ed Lohr. We are both from Rulemaking, Division of Rulemaking, and from the FSME.

Basically, we just wanted to bring back to your attention that the proposed rule, the current schedule is December -- it's due to the Commission December of 2012, and then the final rule is due to the Commission October of 2014. And this schedule we have previously presented at the last ACMUI meeting.

Based on that schedule, we plan to give the draft FRN to the ACMUI for their review, for your review, in July of next year. And as agreed upon -- and it is also in our procedure manual now -- that we would be -- that you will have the full 90 days for that review.

That means that we should be receiving your review and doing our comments on those -- our resolution of those comments in September/October timeframe of next year.

In an SRM to SECY-11-0035 -- that's the one I previously mentioned also a few minutes ago -- in this SRM the Commission asked us to, after the workshops, the staff is to provide the Commission by November 2011 two things. One is an estimate of the overall schedule to complete the rulemaking, and, secondly, any potential impacts the schedule may have on the medical industry at large.

So on potential impacts of this schedule,

we believe the proposed amendments would make clarifications to the rule, consider attestation requirements, and address issues raised in the Ritenour petition. Staff believes that the amendments would make the regulations more effective, efficient, and also enhance safety in certain areas.

Going into a little bit of discussion of that, staff believes that this schedule will have minimal impact, because staff is developing inspection guidance for permanent brachy procedures for the current rule.

And NRC has not heard any instances where licensees indicated shortages of authorized individuals, and those authorized individuals include the authorized users, RSOs, AMPs, ANPs, and so on, due to regulatory constraints. And so at this time, we would like to get ACMUI's comments on the schedule impact.

And just to go back, or just to elaborate, that if we get -- our schedule is based on, you know, we are working on two parts of the rulemaking. One is to do the medical event definition, and then everything else we are calling it as expanded rulemaking. So we are working on the expanded rulemaking, but, as you know, that the medical event

definition was rejected by the Commission last year. And we were asked to go and get that done with the help of the ACMUI.

And, therefore, I have mentioned that -- a few minutes ago that we are counting on that report, so that the staff can use that report, along with the other information they have, to come up with a technical basis for the medical event definition.

So when we go back to the Commission in November, which is, you know, coming up, with our CA note, which is informing the Commission about that -- can we stay with this schedule, or do we need to move our schedule in some other, you know, direction -- so right now we think we can stay with this schedule provided we have that report, so that a technical basis can be developed in a timely fashion.

So having said that, we are just going to note from the ACMUI we are -- we are asking you what you think this schedule of, let's say, the final rule to be in October of 2014, how would that impact license community overall?

CHAIR MALMUD: Thank you. Any comments?

(No response.)

From our experience, we should be able to meet the deadline for the final rule, which is October

of '14. The concern, I understand, is about possible impact on the restrictions of access to AUs for institutions that may be deficient in having them now. Is that what you were addressing?

MS. BHALLA: Yes. We believe that the schedule -- clearly, the sooner rulemaking can be accomplished, the better it is. But we believe that this schedule is not impacting or is not impacting the licensees, because we have not heard that there are any shortages per se.

For example, we have the Ritenour petition, which is also included in this rulemaking. And we believe that although, you know, those RSOs and ANPs, they would like to be recognized and not have to go through the alternate pathway, but we do believe that that pathway is available right now. Although we recognize that it is onerous on the applicant, nonetheless, it is available out there.

So that's what we meant by that we have not heard any instances where there are shortages per se because of this rulemaking, you know, it's not done.

CHAIR MALMUD: Thank you. Has anyone heard of an instance in which there was an actual shortage? Anyone on the Committee? So we -- oh, Sue Langhorst.

MEMBER LANGHORST: Sue Langhorst. I know that there are shortages of radiation safety officers, and we have talked about that in past meetings. But I don't know -- I mean, yes, we would like to have changes done right away, but I think their schedule can't be compressed. I mean, we can say, yes, we need it changed, but this is as fast as we can go on the logistics of what the processes are for rulemaking. Is that correct?

MS. BHALLA: That is correct. I mean, this is -- because rulemaking I think we have -- we have expressed that before, too, it's a process, it's a process by -- we are required to notice for comment, and more complex a rulemaking is -- you need to give that much more time, and now we need to also include this additional time for the ACMUI review.

So not only that we will be getting your review or your comments, then the staff needs to resolve those comments, just like we do for Agreement States or we also do for members of the public. So --

MEMBER LANGHORST: Dr. Malmud?

MS. BHALLA: So it is going to --

CHAIR MALMUD: Dr. Van Decker?

MEMBER LANGHORST: Oh, I'm sorry. Can I follow up, just real quickly?

CHAIR MALMUD: Please do.

MEMBER LANGHORST: I'm sorry.

CHAIR MALMUD: Dr. Langhorst.

MEMBER LANGHORST: Sue Langhorst. I think you see our commitment in how the Subcommittee is willing to go quickly on this report, and the ACMUI not hold you up in regard to getting you that final approval of a final document. So I think you have our commitment to work as quickly as we can on this. So --

MS. BHALLA: Thank you. Ed, do you want to add something?

MR. LOHR: I just wanted to point out, so it doesn't get lost, that the idea of why we need -- the medical event report is crucial is because in our schedule we have already sent to the Commission we are merging that particular rulemaking into the expanded. And that may not be clear as we were presenting that, and I just want to make that point clear.

They merged together, and they are supposed to be released together. And so that's what makes it so crucial for us to get this in the rulemaking process in a very timely manner.

CHAIR MALMUD: Thank you, Mr. Lohr. Dr. Van Decker?

MEMBER VAN DECKER: Well, first, I think we are all appreciative of that, because at one point we heard that couldn't happen. So that's good. But, number two, you know, at the risk of harping on the same subject for a long time, you know, recognize that pragmatically in the trenches 2014 sounds great.

But we are really talking 2017, because that has been my experience from the last rulemaking that started in '97, because the states have up to three years to implement what they see. And many of them took until the last moment on the last go-round, so this is really a long process, and I think the medical event definition, you know, is a pretty big deal.

When you're thinking about it being out there by 2017, depending on the state, that -- so your timeline, I think we are all fine with. The timeline after that on what you could do about that -- that that's what the process is -- is probably going to end up being more frustrating.

There will be states that won't pick up the medical event change until 2017, I promise you.

MS. BHALLA: This is Neelam again. As we said, we are working at the guidance document, and hopefully the guidance document it should help.

CHAIR MALMUD: I was just checking with Dr. Howe. I recall that in the past there was an emergency situation where there was one individual available to be, in terms of AU or RSO --

DR. HOWE: AMP.

CHAIR MALMUD: -- and -- AMP?

DR. HOWE: AMP.

CHAIR MALMUD: And we were able to achieve an exemption by going directly to the district and then to the NRC. So we have not heard of an immediate emergency, but if there were one it could be dealt with. The process is there. It's not pleasant. It's a bit tedious, but it's there, and the exemption can be made in the interim. So we are hopeful that the need won't arise. But if it does, it will not meet a stone wall.

And we, therefore, support what you are doing, and we will try and meet the target. We will assure you we will meet the target that you require.

Thank you. Thank you, both. Oh, I'm sorry. More comments?

MEMBER MATTMULLER: More comments, yes.

CHAIR MALMUD: Okay.

MEMBER MATTMULLER: Hi.

CHAIR MALMUD: Steve Mattmuller.

MEMBER MATTMULLER: Steve Mattmuller. Thinking about what Dr. Hagan spoke -- and I think he was alluding to this, but unfortunately he has left -- but I -- is it possible for the NRC to put out a guidance sooner rather than later in terms of how to define a medical event for brachytherapy, specifically prostate, that is based on activity?

And then, this guidance would accomplish -- because one -- as I think our new future state representative has pointed out, that 2007 team for the current process is when all of this becomes effective. So if we could get guidance out sooner in regards to how this is going to be defined, that that would be helpful for getting more uniform acceptance or interpretation. That's a better word -- interpretation -- of how these -- especially since if it were to be on activity, that's, as I understand it, consistent with the current regulations.

MR. EINBERG: Yes. Chris Einberg here. The NRC recognizes the need for guidance for the existing rule. So do the Agreement States. And there is a joint NRC-Agreement State working group, and it is addressing the issue right now. It is co-chaired by both the NRC and the Agreement States.

The NRC representative on that working

group is Ron Zelac, and the Agreement State representative or co-chair is Chris Timmerman. And so they are actively working on developing something right now, and it is for the existing rule. And their target is to have something drafted by the end of this year. So there are efforts underway right now.

CHAIR MALMUD: Okay. Is there another question, or was it the same question?

MEMBER WELSH: It was the same question.

CHAIR MALMUD: Thank you. It has been addressed satisfactorily for you? Thank you.

MEMBER WELSH: Yes. I'll just say that if guidance can accelerate the whole thing for all parties involved that the Subcommittee report will probably have a sentence or two formally recommending that.

CHAIR MALMUD: Thank you. Again -- oh.

MEMBER MATTMULLER: I'm sorry. One more comment. You mentioned the complexity of the rulemaking or the extent of the rulemaking helps determine the speed of how quickly it goes. And I'm thinking of in regards to the moly-99 potential requirement changes, that since in some ways that is already required by the FDA package insert information, would it be helpful to perhaps cut that

part of the rulemaking out, save it for a later time, if it's deemed necessary? Would that help expedite the other concerns or expedite the rulemaking process?

MR. LOHR: Removing one item from the mount of items that we are considering in this rulemaking would make very little difference.

MEMBER MATTMULLER: Okay.

MR. LOHR: Unless it was one of the very, very major pieces, such as medical event. That might help, but we are not advocating that, but -- and not to downplay the moly, it is very important. But it would make little difference.

MEMBER MATTMULLER: Okay.

CHAIR MALMUD: Thank you. Any other questions for Mr. Lohr or Ms. Bhalla?

MS. BHALLA: Go ahead. Yes, this is Neelam again. Earlier I think there was a question about the public meetings or before we do the final rule after the proposed rule. And it is in our plan right now to have at least one meeting, if not two, before we go for the final rule. So I just thought I will just mention it.

CHAIR MALMUD: And that would be calendar '12 or '13?

MS. BHALLA: 2013.

CHAIR MALMUD: '13, thank you. Thank you, again, both.

And if we may, we'll move on to the last item on the agenda, and that is usually handled by NRC staff. And today Sophie Holiday will address it.

MEMBER GUIBERTEAU: Dr. Malmud?

CHAIR MALMUD: Oh, yes. Excuse me.

MEMBER GUIBERTEAU: Do we have an issue on the table?

PARTICIPANT: We do.

CHAIR MALMUD: We do have an issue on the table? All right. Please remind me. Sorry.

MEMBER GUIBERTEAU: It was regarding the abnormal event -- occurrences, abnormal occurrences, the wording of abnormal occurrence.

CHAIR MALMUD: Yes.

MS. HOLIDAY: I'll address that in my portion.

CHAIR MALMUD: Sophie will address that, she said. Thank you. Thanks for reminding me, Dr. Guiberteau.

MS. HOLIDAY: So coming around to you guys is the recommendation and action items table. So we can go ahead and go to page 2.

All right. Item Number 17. Dr. Welsh, you

asked NRC staff if ACRS members are considered SGEs or SGOs. And, if so, given the number of their Committee and Subcommittee meetings, how many days and hours do they work a year in order to meet those criteria, such as our Advisory Committee?

So we took that as an NRC action, and the answer to your question is that all ACRS members are special government employees. Although they meet much more frequently than the ACMUI does, none of the members exceed that 130-day per year limit. The ACRS staff keeps tabs on the members' days, so that they do not go over that limit, even though they meet so frequently.

However, if a special government employee does exceed those 130 days, the Director of Human Resources has the authority to grant a waiver if there were exceptional circumstances that caused that to happen. However, before that special government employee is reappointed, the office using that special government employee's services should make a determination that that SGE will not exceed the 130-day limit in the subsequent year. Does that clearly answer your question?

MEMBER WELSH: Thank you.

MS. HOLIDAY: You're welcome. Does anybody

have any questions about Item 17?

(No response.)

CHAIR MALMUD: There are no other questions about Item 17.

MS. HOLIDAY: All right. Moving on to Item 18, Dr. Langhorst, you asked that NRC staff provide the ACMUI with Congressman -- or, sorry, provide ACMUI with NRC's response to Congressman Markey's letter regarding patient relief.

Just to verify, Ashley Cockerham resent that email. The email was originally dated January 25, 2011, which contained the NRC's response to Congressman Markey dated January 12th to the ACMUI. And she sent that yesterday evening, on September 22, 2011.

MEMBER LANGHORST: This is Sue Langhorst. I don't think I was the one that asked that, but I very much appreciate that you sent that out. And so thank you. I saw that also.

MS. HOLIDAY: Okay. Great. So I assume there is no question on Item 18.

We can move on to Item 19. Steve Mattmuller asked that NRC staff add ACMUI to the organizational chart on the FSME website, as ACRS is reflected on the NRC website. NRC staff will look into

this.

Are there any questions for Item 19?

CHAIR MALMUD: I see none.

MS. HOLIDAY: All right. Moving on to Item 20, Dr. Langhorst, you requested that NRC staff place historical documents on the ACMUI website, so that viewers could have a better perspective and understanding of the ACMUI's organization.

And in addition to that, you asked that we place past ACMUI members' biographies on the internet, so that people can have a better understanding of who was here before and how we've gotten to here now. So, again, we will also look into this request.

Are there any questions for Item 20?

CHAIR MALMUD: Dr. Langhorst?

MEMBER LANGHORST: I have just one comment. You don't necessarily have to put the biographies on, but it would be nice to name them and what institution -- well, what institution they were from, at least that point in time. So I wasn't asking for a full biography of all --

VICE CHAIR THOMADSEN: And what position they --

MEMBER LANGHORST: Yes, and what ACMUI position they held. That would be very helpful, too.

MS. HOLIDAY: Okay.

DR. HOWE: Do you want that to go back to the very beginning?

MEMBER LANGHORST: This is Sue Langhorst again. The question was whether it went back to the very beginning. Gosh, that would be great, but I know there is limited resources. So, you know, the past 10 years would be nice to have. It would be nice to have a little bit more than that, but I fully understand that is -- that could be a very time-consuming effort. And whatever you could provide, even just going forward, would be great.

MS. HOLIDAY: All right. Thank you.

All right. Moving on to Item 21, Dr. Malmud, you created a subcommittee to address the electronic signatures for documents that licensees are required to retain in accordance with 10 CFR Part 35. I have the Subcommittee members as Dr. Thomadsen, Dr. Suh, Dr. Palestro, and Dr. Welsh. I will need to know who is chairing that Subcommittee.

CHAIR MALMUD: I believe it is Dr. Thomadsen.

MS. HOLIDAY: All right.

CHAIR MALMUD: That's the danger of sitting next to me.

(Laughter.)

MS. HOLIDAY: Are there any questions for Item 21?

(No response.)

Okay. Moving on to Item 22, Dr. Guiberteau, I believe you just mentioned this. So we had a previous recommendation on the table, but Steve Mattmuller and Dr. Langhorst agreed that we should table the discussion on the changes to the AO criteria once we are able to present you with all of the information and facts that you need from the 2008 ACMUI's recommendations.

And at this time, I would like to turn it over to Chris Einberg.

CHAIR MALMUD: Chris Einberg?

MR. EINBERG: Yes. My recommendation is that we combine it with one of the upcoming two telecons that we just agreed to, the telecon for prostate brachytherapy medical events.

We could add this discussion to that telecon, where once you receive the patient release SECY paper and review that and provide your comments, we could -- we will need to have a separate telecon for that. And we could add that to -- this topic to that teleconference. So it's at the discretion of the

ACMUI, which would work better.

CHAIR MALMUD: I think adding it to the existing telecon -- how many hours shall we put aside for the telecon?

MR. EINBERG: Currently, we have two hours scheduled.

CHAIR MALMUD: Will that be sufficient? Dr. Langhorst?

MEMBER LANGHORST: I had a question. I didn't understand -- there are two telecons that are coming up? And so that's where I was confused.

MR. EINBERG: We have not scheduled the second teleconference. We will be providing the ACMUI with our SECY paper on research for patient release within the next month or so. The ACMUI will be asked to review that paper, after which they will need to have a public telecon to receive the ACMUI's views on that paper.

MEMBER LANGHORST: This is Sue Langhorst again. I think it would be good to maybe combine it with that telecon, so that our permanent implant discussions can be pretty succinct.

CHAIR MALMUD: So we will combine them, and we should set aside two hours. Would that be sufficient?

MR. EINBERG: For the -- we are going to combine the AO discussion with the patient release conference call. I believe that that time -- two hours -- probably would be sufficient.

CHAIR MALMUD: We will put aside two hours. When you contract with the telephone carrier, I would book a little extra time if necessary.

MR. EINBERG: Yes, okay. The patient release discussion may require the full two hours, so, yes, maybe three hours would be --

CHAIR MALMUD: All right.

MR. EINBERG: -- better.

CHAIR MALMUD: If you would, though -- we will be on the telecon, we anticipate, possibly three hours. And the time of the meeting will be at noon. Is it not noon?

MS. HOLIDAY: I believe what we are asking is to combine the AO criteria discussion with the patient release SECY paper, which is a separate --

CHAIR MALMUD: All right.

MS. HOLIDAY: -- teleconference. Correct. We did not schedule that as --

MR. EINBERG: And that will not -- Chris Einberg. And that will not be scheduled until we provide you the paper.

CHAIR MALMUD: Thank you.

MS. HOLIDAY: Okay. Are there any questions on Item 22?

CHAIR MALMUD: I see none.

MS. HOLIDAY: All right. Moving on to Item 23, Dr. Malmud added Dr. Suh and Ms. Weil to the Permanent Implant Brachytherapy Subcommittee. Existing Subcommittee members include Dr. Welsh, the chair, Dr. Langhorst, and Dr. Thomadsen.

I understand that, as you have added Ms. Weil to the Subcommittee, she will not be --

CHAIR MALMUD: We have not added Ms. Weil to the Permanent Implant Brachytherapy Subcommittee.

MS. HOLIDAY: Okay. I will correct that on the table. So we just added Dr. Suh.

CHAIR MALMUD: That's correct.

MS. HOLIDAY: All right. Do we have any questions for Item 23?

CHAIR MALMUD: I see none.

MS. HOLIDAY: All right. Item 24, the Permanent Implant Brachytherapy Subcommittee will revise their Subcommittee report and distribute it to the full Committee for review by October 7, 2011.

CHAIR MALMUD: That's correct. They have made that commitment, for which we are very grateful.

MS. HOLIDAY: All right. Thank you.

Item 25, I have that the ACMUI has planned a teleconference for October 18, 2011, from 12:00 p.m. to 2:00 p.m. Eastern Time to discuss and finalize the Permanent Implant Brachytherapy Subcommittee report.

Do I have any questions for Item 25?

CHAIR MALMUD: I see none.

MS. HOLIDAY: Okay. And last item, this is an NRC action item. NRC staff has agreed to provide an advance copy of the Permanent Implant Brachytherapy Subcommittee report to the Agreement States prior to our October 18th teleconference call, and invite them to participate in the teleconference call.

CHAIR MALMUD: That's correct. Thank you. Any comments about that?

(No response.)

We're okay with that.

MS. HOLIDAY: All right. So now we will move on to planning our spring meeting. If you will turn to Tab 19 in your binders. All right. My first set of proposed dates are April 12th and 13th. That's a Thursday and Friday. Does anybody have conflicts with April 12th and 13th?

MEMBER PALESTRO: I do.

MS. HOLIDAY: Yes, okay. All right. The

next set of proposed dates are the 16th and the 17th. Are there any conflicts for the 16th and 17th? That's a Monday and Tuesday.

CHAIR MALMUD: April 16th/17th. Going once, going twice? Sold the whole Committee on April 16th and 17th.

MEMBER MATTMULLER: Just a reminder that everyone has to have their income tax done on the 16th, too.

(Laughter.)

MS. HOLIDAY: All right.

MEMBER MATTMULLER: Bring our checks here and drop them off.

CHAIR MALMUD: Just send in an extension form.

(Laughter.)

MEMBER ZANZONICO: That's my wedding anniversary, but that's okay.

CHAIR MALMUD: Oh.

(Laughter.)

MEMBER ZANZONICO: My wife has given up on those.

(Laughter.)

MS. HOLIDAY: Okay. My next set of possible dates for backup, April 23rd and 24th, also a Monday

and Tuesday.

MS. FAIROBENT: That's ACR's annual meeting.

CHAIR MALMUD: There's a conflict.

MS. HOLIDAY: All right. So that marks that off. How about April 30th and May 1st, another Monday and Tuesday?

(No response.)

CHAIR MALMUD: It looks like there is no objection to it.

VICE CHAIR THOMADSEN: May 1st is not the best. As a backup, I guess it's okay.

MS. FAIROBENT: That's the Roentgen Ray Society's annual meeting dates. I don't know if anyone here is going.

CHAIR MALMUD: Roentgen Ray, May 1st?

MS. FAIROBENT: Yes.

CHAIR MALMUD: It looks like April 16th/17th is ideal.

MS. HOLIDAY: Okay. But I'd like to have a backup date just in case.

CHAIR MALMUD: All right.

MEMBER WELSH: Can I ask --

CHAIR MALMUD: 30th and the 1st. Just --

MEMBER WELSH: Can I ask a question of

the --

CHAIR MALMUD: Of course.

MEMBER WELSH: -- of the members of the Committee? This Thursday/Friday combination seems to work out better for me personally, because I have found that Delta Airlines doesn't have late afternoon flights that it used to have. And so I'm going to have to leave tomorrow morning.

But if it's a Monday and Tuesday, I either would have to leave the next day and then miss a third day of work, or miss part of the meeting. And since I was presenting late in the afternoon, it could have been a problem. So I'm wondering if Thursdays and Fridays is working out better for most of us for the same reason, or Monday and Tuesdays in general is --

MEMBER ZANZONICO: The only thing I would point out is that, don't you miss part of the day traveling Wednesday? This way you would be traveling Sunday. If that kind of balances it out.

MS. COCKERHAM: Dr. Malmud?

CHAIR MALMUD: Yes.

MS. COCKERHAM: Just to make a comment -- the reason we were shooting for the Monday/Tuesday dates, we have requested -- and it has still not been finalized -- we are hoping for an ACMUI-Commission

briefing. In the past, they have taken place on a Tuesday. So if it was possible to have a Monday/Tuesday meeting, that was the push for -- there is the potential to meet with the Commission.

CHAIR MALMUD: So Monday/Tuesday is better for that purpose.

MS. COCKERHAM: I believe the Commission meetings have been on Tuesdays. That has been their preferred dates for those particular meetings. They may come back and say no meeting. They may come back and say, "Hey, we want to meet on a Thursday," and everything I just said goes out the door. But I -- you are welcome to --

CHAIR MALMUD: Is this room available?

MS. COCKERHAM: Is this room available?

CHAIR MALMUD: Maybe.

MS. COCKERHAM: It should be. The first week -- it's the first week of the month that ACRS typically has this room. And we are out -- well outside of that.

CHAIR MALMUD: All right.

MS. COCKERHAM: If you schedule Thursday/Friday, I totally --

CHAIR MALMUD: Do you want a backup of a Thursday/Friday? Thursdays are dreadful for me, but

it's six months, I guess I could change things. Are you proposing April 19th/20th or no?

MS. COCKERHAM: Is that that same week?

MS. HOLIDAY: Yes, it's the same week.

CHAIR MALMUD: Our backup April 19th/20th?

MEMBER SULEIMAN: That's my birthday, so that should be factored into it.

(Laughter.)

CHAIR MALMUD: All right.

MS. COCKERHAM: So what did we decide?

CHAIR MALMUD: And if I have a conflict on the 19th and 20th?

MS. HOLIDAY: I just wanted to throw something else in there. ACRS, they meet on the first and third week of the month, so this would actually be the third week, but they usually have their meeting I believe Wednesday, Thursday, and Friday.

CHAIR MALMUD: So Monday/Tuesday is better.

MS. HOLIDAY: The Monday/Tuesday, if we were to choose this week, the 16th and 17th would be ideal. But the 19th and the 20th would not be for that particular week.

CHAIR MALMUD: Sorry, Jim.

MS. COCKERHAM: There are two rooms, so not -- I don't know that they would be taking up both

rooms, but there is going to be a higher probability that both rooms may be taken.

MEMBER WEIL: What about 26th/27th?

MS. HOLIDAY: Is the ACR meeting the entire week of the 23rd?

MS. FAIROBENT: The 23rd through the 25th.

MS. HOLIDAY: Okay.

CHAIR MALMUD: It looks like 16/17 is the best. Jim? I heard another voice. Did you want to say that for the record?

PARTICIPANT: No.

CHAIR MALMUD: It was off the record. Okay. The 16th and 17th.

MS. HOLIDAY: Okay. So is our backup date still the 30th and the 1st of May, or is May 1st --

CHAIR MALMUD: Backup the 30th and the 1st.

MS. COCKERHAM: I think Ms. Weil had suggested the 26th and 27th, if we were going to do a Thursday/Friday, as a backup.

MS. HOLIDAY: But the ACR meeting is the --

MS. COCKERHAM: Until the 25th.

MS. HOLIDAY: -- until the 25th, so it might be kind of tight.

MS. COCKERHAM: That would be tight schedules for how many individuals?

CHAIR MALMUD: Well, that must be SCAR and the ACR. They usually meet together, right?

MEMBER GUIBERTEAU: No.

CHAIR MALMUD: No? Separate now?

MEMBER GUIBERTEAU: Yes. SCAR is meeting now.

MS. COCKERHAM: Would that be tight travels for you, Dr. Guiberteau?

MEMBER GUIBERTEAU: Pardon?

MS. COCKERHAM: To have the meeting on the 26th and 27th, if you are coming out ACR on the 25th?

MEMBER GUIBERTEAU: Well, the meeting is here in Washington, so that would --

MS. COCKERHAM: Oh, okay.

MEMBER GUIBERTEAU: -- that would work.

MS. COCKERHAM: Okay. So there is your Thursday/Friday backup week?

CHAIR MALMUD: Gone the whole week?

MEMBER GUIBERTEAU: Well, it's not the best, but I'm trying to be -- if you want a Thursday -- we're not going into May, is that what I'm -- okay.

MS. HOLIDAY: We are trying to avoid May.

MEMBER GUIBERTEAU: Well, I think of all those, then the 26th or 27th seems to be the one that

fits with your first and third week of the other meeting.

MS. HOLIDAY: Okay. So does anybody have conflicts with the 26th and 27th?

CHAIR MALMUD: No. I will adjust my schedule.

MS. HOLIDAY: Okay.

MEMBER LANGHORST: And that is the backup.

CHAIR MALMUD: That's the backup, yes, 26th/27th. So 16th/17th or 26th/27th.

MS. HOLIDAY: Very good. Okay. That concludes the presentation part.

Now, just particularly speaking to the Committee, you were given your Form 450, which is a financial disclosure form. I will need that from you at the conclusion of this meeting. However, if you choose to take it home and fill it out, you can mail it to John Szabo, and I will be happy to provide you with his mailing address. But I will need a promise that you will mail it to him.

In addition to that, earlier I distributed your 148 forms for your time and attendance. That is due today, as this is the last day of the pay period. So I will definitely need that today.

VICE CHAIR THOMADSEN: So the periods are

from when to when?

MS. HOLIDAY: Last week was -- yes, September 11th through --

VICE CHAIR THOMADSEN: It's through today or tomorrow?

MS. HOLIDAY: Tomorrow, the 24th.

And, as always, I will email you your Form 64 for your travel vouchers. You can complete those and mail those back to me. All of your instructions will be in my email.

And that concludes my portion, Dr. Malmud.

CHAIR MALMUD: Thank you. I would like to thank all of -- oh, excuse me.

MEMBER WEIL: Before you do, my contact information is a bit old, so I have some business cards I would like to distribute.

CHAIR MALMUD: Thank you.

MS. HOLIDAY: Okay. Great.

CHAIR MALMUD: And I want to thank all the members of the Committee for their effort, talent, contributions, and the members of the NRC staff who have been so accommodating for us.

Thank you all. Have a safe trip home.

(Whereupon, at 4:25 p.m., the proceedings in the foregoing matter were concluded.)