UNITED STATES NUCLEAR REGULATORY COMMISSION

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BRIEFING ON PROPOSED RULE ON PART 35 MEDICAL EVENTS

DEFINITIONS - PERMANENT IMPLANT BRACHYTHERAPY

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THURSDAY,

JULY 8, 2010

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The Commission met at 1:30 p.m., the Honorable Gregory B. Jaczko, Chairman, presiding.

COMMISSIONERS PRESENT:

GREGORY B. JACZKO, Chairman

KRISTINE L. SVINICKI, Commissioner

GEORGE APOSTOLAKIS, Commissioner

WILLIAM D. MAGWOOD, Commissioner

WILLIAM C. OSTENDORFF, Commissioner

ALSO PRESENT:

NRC STAFF

BILL BORCHARDT, Executive Director for Operations,

MARK THAGGARD, Deputy Director, Division of Intergovernmental Liaison and Rulemaking, FSME

JAMES LUEHMAN, Deputy Director, Division of Materials Safety and State Agreements, FSME

ED LOHR, Division of Intergovernmental Liaison and Rulemaking, FSME

RONALD ZELAC, Division of Materials Safety and State Agreements, FSME

EXTERNAL PARTICIPANTS

JAMES WELSH, M.D., ACMUI Member, Subcommittee Chair on Medical Event Reporting for Prostate Brachytherapy, Radiation Oncologist

MICHAEL HAGAN, M.D., Ph.D. National Director of the Radiation Oncology Program, Department of Veterans Affairs

DOUGLAS PFEIFFER, Chair of the Governmental and Regulatory Affairs Committee, American Association of Physicists in Medicine (AAPM)

BRIAN DAVIS, M.D., Ph.D. Associate Professor of Radiation Oncology Mayo Medical School, American Brachytherapy Society

DAVID HOUCHENS, Ph.D. Treasurer, Us Too, International Board of Directors

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

CHAIRMAN JACZKO: Good afternoon, everyone.

We meet today to discuss the draft proposed rule on the definition of medical events as it applies to certain procedures in brachytherapy procedures that we'll hear a little bit more about in the staff and in the stakeholder presentation.

The medical events definition is one of the tools that we use to identify potential problems in a licensee's use of nuclear materials, particularly in the medical arena.

Determining whether the current definition or an alternative definition would be the best approach is really the subject of today's meeting. It's a long meeting about a few words, which, perhaps, is always a good reminder that words are important.

The history of this is somewhat long and has gone back and forth for different ideas.

In 2008, in fact, the agency was proposing a rule that would have changed the criteria for defining a medical event from a dose-based to an activity-based. But as a result of the incident at the Veteran's Administration Hospital, the staff has gone back and reexamined the dose-based criteria, as well.

So, the issues we have in front of us today, as I said, are fairly narrow, but somewhat broad in their application and their impact. So I look forward to a very interesting discussion from the staff and presentations and then from our stakeholders at the end. And I would offer any of my fellow

Commissioners an opportunity to make comments if they wish to. Commissioner Svinicki.

COMMISSIONER SVINICKI: Thank you, Mr. Chairman.

I appreciate your comments about the fact that this may be a narrowly scoped question, but it certainly has the potential to have broad impact. So I appreciate both the staff's input and our external participants in the second panel and I'll be listening very closely to their perspectives.

Thank you.

COMMISSIONER OSTENDORFF: Thank you, Mr. Chairman.

I echo your comments, Mr. Chairman, and Commissioner Svinicki's. I know there's some differences of opinion, and I know that we're going to have some issues here that our job at NRC is to regulate radiological safety for these, these materials, whereas the medical community has a job to practice medicine professionally and competently. I know there's going to be some differences that will come out today, and I just encourage everybody to not shy away from highlighting those differences and why we may be in -- why different organizations may have different opinions.

Thank you.

CHAIRMAN JACZKO: Thank you.

Bill?

MR. BORCHARDT: Thank you, Mr. Chairman.

As you alluded to the development of this rule, as with any change to Part 35 is a challenge because we have the obligation to protect

the safety of the patients while at the same time not intruding on the practice of medicine. It has been a challenge and a longstanding issue for us to arrive at the right place.

In addition to the two presenters today, there's two additional staff members at the table that will be available to help answer questions after our presentation. To my far right is Mr. Ed Lohr, he's a health physicist and the lead staff member for this rulemaking. And then to my far left is Dr. Ron Zelac, who is a member of the NRC medical team.

So, Jim Luehman will begin today's presentation.

MR. LUEHMAN: Mr. Chairman, Commissioners, basically I just want to start on the slide three, a brief history.

In 1973 was when the first medical event reporting rule was proposed. It was called back then the misadministration rule. And it was proposed as a result of a number of medical events that occurred in the late 1960's and early 1970's.

And as you might imagine, given that it was the genesis of the rule, there was a lot of debate about what it should say, and it took basically from 1973 to 1980 to come up with a final first rule, if you will. And that rule, the final rule in 1980 of the final misadministration rule came about after, again, there were a group of medical events that the NRC thought were worthy of knowing about.

Since then, 1987 through 2002 there have been three revisions of Part 35 where, again, we have adjusted the definition of what has to be reported to the Commission as a misadministration or as a medical

event, and those were all done with a lot of stakeholder input, as was the original rule, if you go back and look at the record.

Stakeholder involvement is my next slide.

And obviously, the Advisory Committee on the Medical Uses of Isotopes is a key stakeholder. We solicit their medical advice as most of us, at least, are not medical experts and we value their advice. They give us the medical perspective and we try to factor that in as we make our regulatory recommendations to the Commission.

The medical community at large is also heard on this. We frequently interface with them in drop-ins, we attend their meetings, they come to the ACMUI meetings and interface with the staff and provide their views on various issues, including this, over the years.

Other stakeholders, the biggest stakeholder that I would highlight is that we do look to the international community as well as to what they're doing in these areas. In this area the draft basic safety standards, which are presently out for review, they have criteria in this area and they are dose-based criteria.

The next slide is just a brief summary of the history of reporting under the medical event requirements, and it's kind of a busy slide. But I think the main point that we want to make with that slide is given the number of events, excuse me, given the number of procedures that are performed every year, we have a relatively small number of medical events reported. And that indicates to us two things.

One is, I think, the quality of the medicine that is practiced in

the United States. And, also, I think, as importantly, I think it shows that we have a definition presently which always can be open to a few tweaks when there's, you know, reason to do so, but we have a definition now that strikes a pretty good balance. We are not getting a lot of over reporting of unnecessary events in the staff's view.

And, you know, with that, I would turn it over to Mark who is going to discuss a little bit more of the present rule that's before you and how we got there.

MR. THAGGARD: Good afternoon, Chairman, Commissioners. I just want to spend a few minutes and talk about -- review how we got to the current version of the proposed rule.

First of all, if we turn to slide number six, the purpose of the rule is to determine what actions, if any, is needed to prevent recurrences of events, to make medical licensees aware of generic problems and to allow patients and their physicians to be able to make timely decisions on any follow-on health care that may be needed. Those are the primary purposes of the rule.

I'd like to also point out that our main focus is to protect the patient's health as you mentioned, and so, you know, we try to stay as far away as we can into delving into practicing medicine, but of course there's a balance between the two.

If we can go to slide number seven.

The current effort to revise the medical event definition rule came out of an Advisory Committee on the Medical Uses of Isotopes

Commission briefing back in early 2004. During that briefing, the Commission raised some questions as to whether or not the reporting threshold that we used when you have to make a medical event report, whether that threshold was communicating the right risk information to members of the public.

I think the Commission had some general concerns as to whether or not we were raising unnecessary concerns through the issuance of these medical reports.

So the Commission directed the staff to go back and make a recommendation on a medical event rule. And in SECY-05-0234 the staff came back and indicated that they felt that we had an appropriate basis for the reporting threshold, but the staff recommended that we change our criteria from a dose-based criteria to an activity-based criteria for permanent implant brachytherapy. And that recommendation was made based on a recommendation from the Advisory Committee on the Medical Uses of Isotopes with the primary intent of making it easier for medical licensees to identify medical events and then thus be able to take appropriate actions sooner.

If we can have the next slide.

In the proposed rule that we provided to the Commission in SECY-08-0080, we did put forth a proposal for an activity-based criteria and we also proposed making some changes to the written directive requirements. That proposed rule was published in the Federal Register in August of 2008 and we received 57 comments.

In late 2009 as we were preparing to provide the Commission the final rule, it was discovered that a significant number of medical events that were identified in 2008 would not have been classified as medical events based on the definition in the proposed rule. And that basically came out of reviewing a medical consultant report.

Looking at the data in that consultant's report revealed that in some cases even when a physician were to put the correct activity into the correct organ, you could still not achieve the prescribed dose. In some cases we found that they were off by quite a bit.

So in the re-proposed rule that we provided to the Commission in May of this year, we proposed to retain the activity-based criteria that was in the proposed rule, but we proposed to add back in a dose-based criteria.

Our thinking is that this will still allow medical licensees -- to make it easier for them to identify medical events, but at the same time avoid overlooking the type of medical events that were discovered in 2008.

Can I have the next slide.

So as Jim pointed out, the medical event reporting requirements have a long history. The reporting requirements have been around since at least 1980. As I mentioned, as we've tried to make revisions to the rule, we've tried to balance our need to protect patients' health at the same time while not getting into the practice of medicine, and that oftentimes is a challenge.

We've certainly involved and considered stakeholder input

and we continue to -- we look forward to continuing to do that as we finalize the rule.

That's pretty much our presentation.

CHAIRMAN JACZKO: Thank you.

We'll start questions with Commissioner Ostendorff.

COMMISSIONER OSTENDORFF: Thank you, Mr. Chairman.

Mark, I'd like to go directly to your slides, please --

MR. THAGGARD: Okay.

COMMISSIONER OSTENDORFF: -- and a few questions.

And I appreciate yours and other of your colleagues' comments that you want to protect safety while not intruding on the practice of medicine, and if you do so, it's only based on a well-informed position. So I appreciate your approach and also the approach in the paper.

I wanted to ask a couple of questions that dealt with the issue of flexibility, and certainly the flexibility during the course of a procedure in the hospital or other areas. And I wanted to get your thoughts as to whether or not the proposed rule in SECY-10-0062 has flexibility to allow the medical practitioners, the authorized users to adapt to the circumstances as he or she sees it in the procedure room where this is being accomplished?

MR. THAGGARD: Well, I can give my opinion and then maybe I can ask Dr. Zelac to see if he has an opinion on it.

I think there is some leeway within the rule, I think there's some provisions in there that the physician can make oral changes to the written directive at certain points during the procedure.

So, I don't know, Ron, if you want to weigh in on that.

DR. ZELAC: A lot of the objections that came from the medical community said that the work-ups for patients occurred at a significant time period before the actual treatment began, and the changes that would take place in a patient's anatomy, for example, would make it inappropriate to follow the original plan without making modifications to it.

We have in the current rule, and we would have in the re-proposed rule, an ability for the physician to make a change in the written directive up until the very last minute before the procedure begins. So that when they have the visualization that occurs before they start to implant seeds and see that things are different than they had been previously, they can make appropriate adjustments both in terms of the amount of radioactivity that they estimate will be necessary as well as, of course, the placement of that activity within the patient.

Secondly, once the procedure has begun, there can be continued modifications that occur in patient anatomy due to swelling, for example, of a gland.

We have -- we've put that question to some medical practitioners of high esteem and what we received back from them was that our proposed variance limit of plus or minus 20 percent was sufficient to take into account the additional modifications that might be required once the procedure begins.

COMMISSIONER OSTENDORFF: Do you feel like as you and your team have looked at these various issues that you have -- this word

intentionally -- a consensus view from the medical practitioner community that you can understand where the practitioners are or are their significant differences from where you sit between one practitioner organization and another?

DR. ZELAC: I think that there are, there is sufficient variation in views that it's challenging to come up with something that would satisfy everyone.

COMMISSIONER OSTENDORFF: All right. Thank you.

Let me -- thank you, Doctor.

And, Mark, a question on the written directive being completed and so forth. And I understand that there are caveats in there that if a written directive were not completed and if the underlying medical information that was available did not allow an assessment of whether or not there has been a medical event, that that would possibly trigger a medical event.

And I wanted to see, you know, is that something that -- do you see that there's a large number of these cases occurring or do you have any imperial data that would help inform us as to the prevalence of this being the situation, where written directives should have been completed but were not?

MR. THAGGARD: Yeah. Let me see, Ed, do you have an opinion on that?

MR. LOHR: Actually, during the history -- as we do a proposed rule we do a complete history of how we got to where we're at.

Looking at that, there was a couple of cases several years

ago where this exact thing occurred where they had the procedures occur without a written directive.

And under current regulations and under the re-proposed rule the basis for a medical event points back to what the physician intended for the patient to receive, and that's what's in the written directive. Without that written directive there is no basis to determine whether anything went astray.

And so what we in the working group did was look at this issue and determined that perhaps it would be a good place for the NRC to be is to have those reported to us.

Now, we also put a provision in there if there's particular information in other records such as patient records or in other, other sorts of records, that could be used to determine if a medical event had occurred, they could use those in lieu of the written directive.

COMMISSIONER OSTENDORFF: Thank you.

Thank you, Mr. Chairman.

CHAIRMAN JACZKO: Commissioner Svinicki.

COMMISSIONER SVINICKI: Thank you.

We will hear in the next panel from a member of our Advisory Committee on the Medical Uses of Isotopes, but I'm less familiar -- ACMUI is a staff advisory committee, I'm more familiar with our advisory committee on reactor issues, so -- since that's a Commission advisory committee. But when we get an ACRS report, we get the benefit of a response from the staff so we can see how the staff has addressed the issues that the ACRS has raised.

I'm not familiar with our practices with the ACMUI. When they

transmit a review or comments on something, does the NRC staff provide any kind of a written comment response to those comments?

DR. ZELAC: During an ACMUI meeting there's a full record kept of what has transpired, which would include the specific recommendations that have been approved by the ACMUI.

There is follow-up that takes place for each and every one of those recommendations, and the follow-up that does occur is documented, and that is at least sent to the Chairman of the ACMUI, and I'm not sure what the distribution is beyond that.

So to answer the question specifically, yes, there is follow-up and yes, there is documentation that is given back to the group that created the recommendation to begin with.

COMMISSIONER SVINICKI: Okay. My understanding is that the ACMUI comments that they will send to the staff on the medical event definition -- and perhaps those are encompassed in broader comments on the re-proposed Part 35 -- my understanding is that their report is still in draft and, again, they're on the next panel and so I can ask that question.

But getting back to the staff's practice, it would be upon receipt of any of those comments, it sounds like there would be the formality of a written response to the staff that would react to any proposed changes that the ACMUI suggested?

DR. ZELAC: If the recommendations that come from the ACMUI relate to a rulemaking, that information would be conveyed to the appropriate rulemaking working group.

In addition, the ACMUI, as everyone else, has an opportunity to formally submit their comments once the proposed rule has been published in the Federal Register, and they have done so in the past.

COMMISSIONER SVINICKI: Okay. So the -- it sounds like the point that we're at right now is obviously the Commission has before it the re-proposed rule for its review. I'm not certain of the timeframe for the ACMUI submittal and I certainly will ask that of the next panel.

But, it sounds like the staff would then take that into consideration, it wouldn't be part of the public comment record, it would be separate from that? Or I suppose they could take the same comments and submit them in either forum?

DR. ZELAC: The approach that has been taken in the past, as I noted, was to receive the comments and to integrate them in the production of a proposed rule. But even when that is done, the ACMUI then still has the opportunity essentially, perhaps, to change its mind, as it has done on occasion, and submit comments which are essentially counter to the recommendations that they have made in the past.

COMMISSIONER SVINICKI: I suspect we'll be hearing in the next panel some of the concerns and differences that the ACMUI may -- again, I don't think they've completed their work on these comments yet, but it sounds like from what you are confirming of my understanding of the processes, we're not going to be in a position for the Commission to have the benefit of the staff's rebuttal, if you were, to the ACMUI suggestions for changes in the re-proposed rule.

And so what I'm trying to do is think about how we could get

these processes in sync, and it may be that we can't. Of course the Commission has not acted on the re-proposed rule yet. But again, I point out only for myself that I benefit in terms of the ACRS of knowing what staff's response is to the ACRS' concerns, and in this case I guess I may find myself having to vote on a matter without that sort of benefit of knowing the staff's response to the ACMUI concerns. So, I guess I'll ponder that a little bit more.

But if there were some way for the staff to transmit to the Commission, it may be that that would be helpful to know if we're in receipt of the ACMUI's concerns, which may be very substantive, it may be helpful to know what the staff's response is to any of these issues.

MR. THAGGARD: Well, if I can say something, Commissioner, remember the rule hasn't gone out for public comment yet, so whatever comments we receive, we will respond to those. So certainly whatever comments we get from the advisory committee would be considered part of the comment response. So you would at some point get the staff's response on those comments.

COMMISSIONER SVINICKI: And again, I don't mean to belabor it, but I think what I'm commenting on is the uniqueness of my position of having to perhaps act on this re-proposed rule without the benefit of the -- I will have only the incoming concerns and not the staff's response to that. And then the uniqueness of the ACMUI. They do exist as an advisory committee, so even a rule that's not out for public comment could have the benefit of their informed medical opinion, which I'm not sure that the proposal before me right now has the

benefit of. But I'm over my time.

Thank you.

COMMISSIONER APOSTOLAKIS: Thank you, Mr. Chairman.

Please go back to slide five where there is a list of – the total medical event reports.

I'm wondering how many of these actually harm the patient, do you know?

MR. LUEHMAN: That's not a determination that we make.

We, typically in the -- when we have a medical event, we do get a -- we employ a medical consultant to review the event.

In many cases I can say that given the condition of the patient that was involved, if there are adverse effects seen in the patient, the medical consultant will give us a view, but a lot of times it remains indeterminate whether the -- even in some of the most significant events, whether the actual procedure caused those symptoms or problems or whether it was the underlying disease. So it's a very difficult decision to render on the part of a physician looking at it after the fact, given the condition of many of the parents that are involved in these.

COMMISSIONER APOSTOLAKIS: But you just used the words "most significant." How do you decide what is most significant?

MR. LUEHMAN: Well, I think that I would say most significant as being events -- typically when you're looking at adverse effects, that it's going to probably be due to an event where there's an overexposure rather than underexposure of the patient, or exposure to unintended areas or organs as

opposed to an under dose to the organ that it was supposed to be delivered to.

And obviously when I mean most significant, I mean significantly outside the 20, the plus 20 percent dose that's allowed under the rule.

COMMISSIONER APOSTOLAKIS: I guess, not I guess, I know why I'm asking these questions.

I mean what kinds of risks are we dealing with here? I mean is it life and death or minor injury, or what?

MR. LUEHMAN: Ron?

DR. ZELAC: The two considerations are first, if the dose is much less to the treatment site than had been planned, the treatment has the possibility of not being effective. Typically the therapies are for cancer and the cancer may not diminish or may recur. So there's the risk side on the low.

On the high side, we can have damage to adjacent critical organs. If the dose to the treatment site is significantly higher than had been planned, then the doses nearby are also higher than had been planned and they can be significant in terms of damage to those surrounding critical organs, because typically it's right at the edge that you try to work, as much dose as you can give without damaging normal nearby tissue.

COMMISSIONER APOSTOLAKIS: So, if it is beyond the 20 percent of the prescribed dose on the high side, we don't necessarily have harm immediately, right? It could lead to some harm, but not necessarily?

DR. ZELAC: But not necessarily.

There are certainly some of the medical events that are listed

in that slide for which we know that there was damage, physical damage, to the patients involved, skin burns, for example, from a source that's misplaced.

COMMISSIONER APOSTOLAKIS: Okay, what do we do with these reports by the way? I mean do we have a decision-making process where we evaluate them individually and deciding what to do?

Mark mentioned the primary purpose is to prevent recurrence. Is that the only thing? I mean are we imposing penalties, for example?

MR. LUEHMAN: No, sir. We do a number of things with them.

Like I said, we have evaluation by our own medical consultants that we bring in to look at the events. We ensure, as Mark, consistent with what Mark said, that when a hospital or a medical provider has an event, that they have taken the appropriate corrective actions, whether that's retraining, whether that's improvement of their procedures.

We look for extent of condition. Was this just a one-time event due to a bad placement, due to malfunctioning equipment, maybe a bad scan in preparation for the event, and we get the licensee to correct that to the extent it needs to be corrected.

And then the third thing we do, we do trend all of our, not only our medical event report data, but all our materials' event data looking for trends and looking for new types of events.

One of the things that you have in the medical community is you have a rapidly changing set of modalities that are applied. And if you have a new procedure that's used, is being used in the community and all of

a sudden you see some medical events in that area, that would cause us to focus more attention, especially if it was a new type of modality that did not have a long track record and all of a sudden there was, right off the bat there were a large number of events.

Or, if you have a long, if you have a modality that's been around a long time and all of a sudden there's a spike in events, maybe there's an issue with, which we've seen, software or hardware with a machine maybe after 15 or 20 years. We are looking for those.

Now, as I said when I talked about my slides, the difficulty in this area is the medical treatment that's given in this country is very, very good. And, therefore, we see very few medical events. And so looking for these trends or looking for these anomalies is very difficult given the small percentage of procedures that actually lead to significant adverse outcomes.

COMMISSIONER APOSTOLAKIS: Thank you, Mr. Chairman.

CHAIRMAN JACZKO: Commissioner Magwood?

COMMISSIONER MAGWOOD: Thank you, Mr. Chairman.

Let me first thank the staff for the work they've done on this and thank Dr. Zelac for his information he provided me yesterday, it's been helpful in understanding this issue which is obviously not exactly in our normal venue of reactors and materials licensees, it's a little bit different territory.

Let me ask -- let's talk a little bit about the medical events, because you've made reference to the number of medical events in a couple of different ways.

I think in your presentation you spoke about the fact that we don't have an inordinate number of medical events, so, therefore, the system is working. And I think you also have that -- or I think the staff has said on several occasions that one concern about the original proposed rule was that had it gone into effect, the number of medical events would have dropped because we wouldn't have recognized events as being medical events, they would have simply been falling off the charts, so to speak.

But the number of medical events seems to have been redefined somewhat here as an objective unto itself and I want to ask a little bit about that.

Medical events basically exist as an artifact of the regulatory system, correct, they don't have particular meaning in the medical community, is that an accurate statement?

MR. LUEHMAN: That's correct.

COMMISSIONER MAGWOOD: Okay. If what we're trying to do is to -- if your sense is that if we had gone to the original proposed rule, the activity-based rule and the number of medical events had gone down, and you said, and I think the staff reaction was that's a bad thing, we would be missing some medical events, if the medical events don't have a medical meaning in terms of what the physicians are looking at, how should the Commission look at this?

It seems like we're being told on one hand that we want to protect the patients, but we don't want to practice medical, but we're creating an artifact, medical events, which seems to be substituting our judgment for

the judgment of the physicians.

And I, I don't want to sound like I'm challenging you on this, I just want to understand this a little bit.

MR. LUEHMAN: I think that's a good question, and I think that all one has to do is to look to the recent reports that have been in the media concerning machine-based radiation.

There have been a number, there have been a lot of articles in that area, and the threshold in that area, where there is a threshold, is death or serious injury. That's where the required reports have to be made, for instance, to the FDA by a machine manufacturer.

It's the staff's view that if we are reporting when -- if reporting starts occurring only at death or serious injury, that we are not at the right place in a regulatory manner.

We should see those events that are outside what would be reasonable practice, as Dr. Zelac referred to, plus or minus 20 percent on this, on brachytherapy as the threshold, and it's our view in having consulted with the medical community that if you're not getting results that are within that range, that there is some potential problem, not necessarily an actual problem, but a potential problem with procedures or training that is worth looking into before we get to the point where we have death or serious injury. And that's what we're attempting to do.

COMMISSIONER MAGWOOD: But I guess what I hear you saying, though, is that even, as you look at medical events -- and I think in your discussion with Commissioner Apostolakis this came out -- that medical events in

and of themselves are not necessarily harmful. In a medical event a variance from the written directive doesn't, -- a single medical event doesn't necessarily have to be a bad thing, it's simply a variance from the plan.

So I think the one question that we should be asking is -- and let me say that Dr. Zelac and I talked about this a little bit yesterday and it was clear to me that the staff understands that medical events are not necessarily harmful. They could be harmful. But what they are is a way of measuring a trend of practice as opposed to measuring the effectiveness, necessarily of treatment.

So again, it seems like we've overlain a regulatory structure on a medical procedure, and it seems to me that the regulatory structure is pushing on the medical procedure, and the question is, is it pushing too much or is it pushing enough, and I think that's a judgment we have to make.

I'll sort of end with this because I know my time is running out, but we'll have an opportunity to talk with the other panel about this. But if you have any final thoughts, I'd appreciate hearing them.

MR. LUEHMAN: No, sir. The only thing I would say is that the philosophy that we -- the general philosophy that we attempt to impart here as far as reporting is very consistent with what we do in reporting in other venues that the NRC regulates, whether it be with radiographers, whether it be with reactor licensees on their events. We don't wait until there's -- our requirements don't cut in when there's only an actual problem that has significantly adverse results. They come in, our reporting requirements come in some time before that, and it's a judgment that I think we've gotten pushed back from all the regulated

communities as to whether that judgment has been put in the right place. And I think we will continue to do so as we are the regulator and they are the regulated community.

COMMISSIONER MAGWOOD: Thank you, Chairman.

CHAIRMAN JACZKO: Well, to follow up on that. It's clear, and sometimes the English language is unfortunate because the, "e" could stand for event or it could stand for error, and it appears that sometimes there's a confusion that a medical event is a medical error, which it's not. I think Commissioner Magwood raised that question and you answered that, Dr. Zelac.

But more importantly, and I think Commissioner Apostolakis or Commissioner Ostendorff raised this too, if I understand it correctly, it's not a violation either, necessarily, it's a reporting requirement; is that correct?

MR. LUEHMAN: It's only a violation if it's not reported. Now, there may be underlying violations of other requirements. But if a medical event occurs and it's properly reported, in and of itself it's not a violation.

CHAIRMAN JACZKO: I think that's -- again, as I've talked to people, it seems to be, again, part of the challenge we have here is that there is a communication challenge, I think, with having people understand that fact that it is not -- we're not talking about a -- it's violated if you don't do the reporting, it's not violated by satisfying the criteria, or there's no safety violation by satisfying the criteria. There is a reporting need to alert us of issues.

Is this the only type of procedure in which we use a medical event

definition with a 20 percent variance?

DR. ZELAC: No, absolutely not. The plus or minus 20 percent applies across the board to the medical event reporting criteria for all modalities and treatment.

CHAIRMAN JACZKO: In all those other modalities, it's a dose-based --

DR. ZELAC: That is correct.

CHAIRMAN JACZKO: In any of those other modalities do we have a similar problem with the definition being used and understood and accepted?

DR. ZELAC: We have not.

CHAIRMAN JACZKO: In your mind is there a particular reason why with this procedure there is this divergence of opinions?

DR. ZELAC: I would attribute it to the fact that in this procedure there are, there's less control of the physician over the result than there is in other procedures that are utilized.

CHAIRMAN JACZKO: And as I was reading some of the research, I noticed there was a, there was a, a journal article -- and I have to admit I don't routinely read Medical Physics, I think this is the first time I ever read an article from Medical Physics. But there was an article talking about, it was in AAPM, the American Association of Physicists in Medicine recommendations in dose prescription reporting methods for permanent interstitial brachytherapy for prostate cancer. They were talking about this and there was an interesting comment they made that they said that most

inconsistencies in dose reporting are a result of disparity in target delineation.

Would you agree that that's largely, or any of you, for that matter, that that's largely where the difficulties are here in delineating the dose is that because it's difficult to determine where the prostate is in a procedure, where the prostate stays or how it doesn't change?

DR. ZELAC: I think that that is clearly one of the difficulties involved in part because, first, there's a different imaging modality that's used typically during the treatment than there is used afterwards for the dose assessment. And secondly, because of the fact that different clinicians, based on their experience, will visualize the target differently and create the boundaries of it differently. That's one of the contributors to this problem. The other is the time at which the dose determination is made.

If, for example, the determination were made very shortly after the procedure was conducted, there is a strong probability that the resultant computed dose will appear to be low because of possible swelling or actual swelling that occurred in the treatment site during the implantation procedure itself.

However, if there is, following the recommendations that are in that report, determination of the dose at an appropriate later time after the procedure, it's very much more likely that the result will be in line, or certainly much closer in line with what had been intended.

CHAIRMAN JACZKO: And that's the reason the staff put in the 60-day window in which to do the dose calculation?

DR. ZELAC: With the activity-based portion criteria there is a

clear need for defining, because the current rule does not, when the procedure is completed, and for making determinations as to, one, how much activity was placed and where it was placed that's -- excuse me, before the patient leaves the post treatment recovery area. So that's a determination that can be made very quickly.

But the other aspect of it is when should the dose be determined? And because the recommendation for the longest lived radionuclide currently in use, i25 is 60 days and the dose determination as recommended in that report was to be made at 30 days, give or take a little bit, we decided that 60 days was an appropriate time to allow for, for example, the patient not being available to come in at the appropriate time. But there is -- that's the time cutoff and when essentially the procedure is completed, when the dose that was delivered is determined.

CHAIRMAN JACZKO: Okay. So it's not an instantaneous, I mean that accounts for the issues of swelling and all these other effects that make it difficult to, to determine the target volume?

DR. ZELAC: There will be variations, as I said, that occur in the treatment site itself in terms of its size, and that, of course, will affect the dose. So the, the best determination is made at the appropriate time depending on the radionuclide that is in use.

CHAIRMAN JACZKO: Okay. Thank you, I appreciate that and I appreciate the staff's input here.

We, we will have another panel, I think we'll have some additional perspectives and I think it will make for a very interesting discussion for the

Commission.

Thank you.

(A pause in the proceedings.)

CHAIRMAN JACZKO: I thank everyone on our stakeholder panel for being here, we, we have a very distinguished group of individuals to share with us their perspectives on, I think as Commissioner Magwood put it, the nexus between the regulatory function that we play and the medical practice that many of you are involved in.

We will begin with Dr. James Welsh, who is a member of the Advisory Committee on the Medical Uses of Isotopes. He's the Subcommittee Chairman on Medical Event Reporting for this particular issue. We'll then turn to Dr. Michael Hagan who is the National Director of the Radiation Oncology program at the Department of Veterans Affair. Then we'll hear from Douglas Pfeiffer who is the Chair of the Governmental and Regulatory Affairs Committee at the American Association of Physicists and Medicine. Then Brian Davis who is an Associate Professor of Radiation Oncology at Mayo Medical School and member of the American Brachytherapy Society. And finally we'll hear from David Houchens -- is that --

DR. HOUCHENS: Houchens.

CHAIRMAN JACZKO: Houchens, sorry -- who is Treasurer with Us TOO International and on their board of directors.

We begin with, with Dr. Welsh.

DR. WELSH: Thank you, Chairman Jaczko.

I will be giving my perspective today as Chairman of the

Subcommittee on the Permanent Implant Brachytherapy of the ACMUI as well as an authorized user, radiation oncologist, with vast experience with real time prostate interstitial brachytherapy, among other modalities.

As you mentioned, this is a long meeting about a few words, and those few words are “medical event.”

So if I can have my first slide.

What is the purpose of defining a medical event?

Well, there are two general purposes.

One is to identify trends and patterns so that corrective actions may be initiated before the events actually occur. In my opinion, it might be reasonable to categorize this as something else, “regulatory event,” for lack of a better term, and reserve “medical event” for those events that are truly of medical significance.

In any case, defining a medical event is something that necessities a very careful balance. We want to avoid being overly sensitive in our definition and thereby capturing many clinically insignificant events and thereby overburdening the system.

As an aside, the re-proposed rule has been criticized in that it may capture far too many events than it was originally intended to, some have estimated thousands.

This has to be balanced by the assurance that the definition will indeed identify those procedures that are potentially harmful. This is a very difficult task, everyone wants to get this right.

The subcommittee believes that the re-proposed rule in its

current form falls a little bit short in this challenging balancing act.

Next slide.

An appropriate definition of a medical event is one, in my opinion, that reflects true potential harm to a patient. Harm to a patient --

This may be the slide before it. Thank you.

Harm to a patient can be overdosing normal tissue which causes direct radiation injury, but also under dosing the target and thereby not curing the patient.

Again, this requires another very careful balancing act. And it is worth keeping in mind that prostate brachytherapy is a very safe and proven effective modality for dealing with prostate cancer. It would be a shame if this modality became unavailable to patients who could benefit because of overly restrictive regulation.

Going on to the next slide, there are inherent difficulties with coming up with an appropriate definition for medical event in prostate brachytherapy.

Brachytherapy is a bit of an art, an art of medicine, and by this I mean the art of sparing the urethra during prostate brachytherapy procedure, or sparing the anterior prostate when it is possible, or intensifying dose to an area that is identified in the operating room as a nodule in the prostate, for example.

These are done on the fly, real time and it appears as an art, but it is an art that is scientifically based. Therefore, no simple definition of medical event adequately covers all potential adverse circumstances, at

least no simple definition that has been proposed thus far, including that in the re-proposed rule.

The ACMUI may be able to assist in refining the re-proposed rule and coming up with medical definition that does accommodate this.

Next slide.

Some of the challenges that have already been alluded to include challenges to a dose-based criteria, and the subcommittee acknowledges that dose-based criteria may be appropriate and necessary in certain rare situations, such as if all seeds are bunched into one single location.

This is a medical event in most practitioners' opinions, but it is not captured by the previously ACMUI proposed rule. On the other hand all previously proposed dose-based criteria create new difficulties and challenges.

Next slide.

A difficulty that has already been alluded to in any dose-based calculation or definition of medical event is that the volume changes. The volume can often increase from edema after numerous needle sticks and foreign bodies implanted. The prostate, as an example again, often shrinks after the procedure because of hormonal therapy and atrophy from the procedure itself. I call these anatomic volume changes.

There also are volume changes that occur that are not truly anatomic and can affect the calculated volume.

In the way of background: There are things called

patient-related factors such as if a temporary implant is pulled out by a patient, or if a seed migrates out of place after it has been placed correctly, or if stasis occurs during a Y-90 microsphere procedure. These are beyond the authorized user's control and are not categorized as medical events.

We would propose that edema and shrinkage which affect volume and which therefore, by definition and geometry, affect dose, be excluded from medical events because they are beyond the control of the authorized user. They should be categorized as patient factors.

Next slide.

So, a proposed concept is that if a dose-based criteria is used, we suggest the concept of introducing normalization to V(init), the volume that the authorized user originally planned the treatment on. Why? Because there can be differences in the volumes calculated: Ultrasound versus CT versus MRI, modality-based challenges; interuser differences in contouring and intrauser differences in contouring which have been documented; artifacts secondary to the numerous seeds that are placed in the prostate. These pose challenges that cause non-anatomic volume differences.

Next slide.

The V(init) concept can be easily implemented because it is known for all procedures and it does not require additional effort.

The next concept that the subcommittee discussed was to properly address medical events we have to have a good definition of the treatment site.

What is the treatment site to an authorized user?

Next slide.

This is a slide that you're all familiar with, you've seen many times. We again recommend appropriate terminology be used, gross tumor volume, clinical target volume and planning target volume, which one is truly the treatment site?

Similarly, if we're defining a medical event based on dose, the dose as a number, plus or minus 20 percent, but what is this number? Is this the V90? Is this the D90, the V100? We need to be more precise in our definition of the anatomy and of the dose.

Next slide.

The subcommittee was divided about the insistence on post-implant dosimetry as a medical event. We all agree that it should be done, but it would be a moot point if dose-based criteria was not adopted. And there was some debate about whether it should really be used for regulatory purposes in the definition of medical event. Again, if there was something called regulatory event, it might solve the problem.

Next slide.

So, some final thoughts. If we return to the concept of a medical event as something that is truly of potential harm to a patient, number one, a solution could be to shift the emphasis and focus more, or at least equally, on dose to normal tissue.

This is not a new concept in NRC, it's used in other areas, and this would adequately address the goal of identifying potential harm to

parents in that overdoses to normal tissue, that is absorbed dose that exceeds normal tissue tolerance, is potentially harmful.

Number two, the ACMUI also has a suggestion that would address harm due to under dosing of the target and therefore not curing the patient.

Next slide.

In conclusion, the ACMUI subcommittee is presently opposed to certain aspects of the re-proposed rule and does not urge the Commission to publish it in its present form. The matter is very complicated and it would be reasonable to have -- and it will have a huge impact on the regulated community.

Next slide.

So it is imperative that we get the ultimate version of this rule as close to perfect as humanly possible, and the present version of the re-proposed rule fails in too many regards.

We recommend that NRC seek stakeholder input during any revision of the re-proposed rule. And, finally, if NRC desires a dose-based criterion, the subcommittee is prepared to offer an understandable, unambiguously measurable and carefully considered solution based on all of the above.

Thank you.

CHAIRMAN JACZKO: Thank you.

DR. HAGAN: Good afternoon, Mr. Chairman, Commissioners, thank you for this opportunity.

First slide, please.

The metric for assessing prostate dose must be with high physician to physician reproducibility, able to isolate undisputedly bad implants. Capturing acceptable implants that could be better is an intrusion into the practice of medicine. It's a de facto effort to regulate not only safety, but quality as well.

By requiring absorbed dose metric without the specific allowances that Dr. Welsh has mentioned from the ACMUI reposition for a prostate dose of a volume implant forces the NRC to direct the practice of medicine.

It's the purpose of the regulatory evaluation to determine whether the authorized user has used byproduct material as intended.

To accomplish this task, 10 CFR 35 details requirements both for written directive and post procedure dose evaluation.

The second slide.

By rule, the specific regulatory element which we have discussed now is plus or minus 20 percent of the dose prescribed, while other organs and tissues are held to less than 150 percent of their expected doses.

A quite natural follow on for these requirements is the desire by the regulator to know both the intended radiation absorbed dose and the actual dose resulting from the placement of the regulated material.

Indeed, the Veterans Health Administration's Blue Ribbon Panel recommended the use of routine dose volume histogram analysis,

which is absorbed dose measured, to determine dose delivered to other organs and tissue.

This is not the case, however for the prostate itself.

In 2005 ACMUI correctly advised NRC that for this regulatory evaluation, no absorbed dose metric could be simply applied to a volume implant such as permanent interstitial implant of the prostate.

The explanation for this category rejection is fourfold: First, as you've heard, an absorbed dose received by the target volume cannot be determined with acceptable precision, it can only be estimated.

Secondly, the authorized user cannot control the absorbed dose during the period when the estimate is obtained.

Thirdly, due to intentional heterogeneity of the physical dose distribution, no absorbed dose measure of peripheral dose reflects dose within the treatment site with a range even close to the regulatory language, plus or minus 20 percent.

Fourth, during post implant dose assessment you have heard that clinicians vary considerably on their delineations of the target for prostate treatment site, which markedly alters any measure of absorbed dose. Specifically the absorbed dose of prostate is a target volume dependent parameter, and this target volume varies substantially during dose delivery.

While the median increase in prostate volume due to edema has been estimated to be in the neighborhood of 50 percent, the range extends from zero to 200 percent. And while the resolution of this edema

has been estimated to have a median half-life of 10 days, it may vary from four to 26 days.

Consequently, dose measurement on a single day of a volume trajectory provides only a point estimate. How closely this estimate actually approximates the absorbed dose depends on the residual edema at the time of the estimate, which is not in the control of the authorized user.

On slide three, notice here that the prescription dose and the isodose which defines a medical event are one to three millimeters apart on this day, for this particular prostate, the prostate has increased in size by 50 percent over its size on the morning of the implant. Its diameter has expanded by nine millimeters, over three times the distance between these critical isodose contours.

Finally, focusing on a 20 percent limit around a minimum peripheral dose estimate overlooks inevitable and constantly changing realities at any moment, as is true for that prostate you were seeing on the last slide, greater than 50 percent of the treatment volume is actually receiving over 150 percent of the prescription dose. In fact, a significant portion of that volume was receiving in excess of 200 percent of the prescription dose.

Moreover, in a given clinical scenario, practitioners intentionally vary the amount of tissue they want to cover.

And the next slide, the clinician has decided to reduce the anterior coverage for this particular patient with scant volume of low risk disease, and yet regulators looking at this implant prefer to evaluate it for

uniform coverage by minimum peripheral dose to the entire CT volume, which caused this to a medical event.

The patient is, by the way, doing very well with a low PSA many years later.

It follows then that a clinical outcome -- if you'd leave the last slide on for a second.

It follows then that clinical outcome cannot be directly and closely related to any single measurement of absorbed dose. As a result, some clinicians are more interested in source distribution with respect to likely tumor locations for a given patient or presentation than obtaining a certain minimum peripheral dose to uninvolved regions of the prostate.

On this last slide, the pathologic distribution of disease seen on your left correlates pretty well with where this physician has decided to place seeds for this particular patient.

Requiring practitioners to obtain a specific minimum peripheral absorbed dose for the prostate, the regulator directs the practice of medicine. Regulators should focus on the original task of determining whether the authorized user has used byproduct material as he intended while avoiding parameters uniquely within the expertise of the authorized user.

Using available technology, the authorized user can control with acceptable accuracy the initial anatomic placement of the source material.

That's it.

Regulatory limits must themselves be limited by the predictable deployment of the isotope. The authorized user is required to verify that more than 80 percent of the dose was applied to the treatment volume.

On the next slide you'll see for these procedures, 10 CFR 35.2 defines dose by source, strength and time in addition to absorbed dose.

Assessing that sources were delivered where they were intended to be delivered is sufficient for effective regulatory oversight.

That NRC and Agreement State counterparts would attempt to fully manage or control the complex matrix of local biology of the recently implanted prostrate has no precedent. Regulatory organizations have neither the experience nor the appropriate training credentials for these decisions.

Therefore, on behalf of the entire radiation oncology community and our collaborating urology colleagues, we urge the NRC to focus on the appropriate areas of training and skill which can continue to be a very effective voice for the safe use of therapeutic radioactivity.

Last slide shows in conclusion.

Once it's determined that the placement of source material has followed the written procedures, including the written directive, how dose develops from that distribution, how in turn that delivered dose removes disease and produces toxicity is the responsibility of the physician, it's not the province of the regulator.

As you read those conclusions, I'll note that a reanalysis using

V(init) as has been described by Dr. Welsh from Philadelphia shows that two-thirds of the implants that failed a regulator imposed D90 criteria actually were fully in compliance with the radiation therapy oncology's clinical group criteria for phase three protocol acceptance.

CHAIRMAN JACZKO: Thank you.

Mr. Pfeiffer.

MR. PFEIFFER: If may I have my slides, please.

Mr. Chairman, Commissioners, thank you for inviting us here today.

I am representing the American Association of Physicists in Medicine.

May I have my slide, please. Go to the next slide.

I wanted to address, generally, point by point the suggestions that have been made and offer some additional information and some suggestions that came up through conversations today and listening to what others have said.

In a general response, when I was reviewing our 2008 comments, the NRC staff did make an effort to address all of those, and we do commend staff for having tried to address all of those in some manner in the best way they can.

We understand that you are attempting to balance needs of both conventional preplan and real time planning, when we're talking about prostate implants, along with other implant procedures. And trying to have one rule that encompasses all of those is very challenging, and I think that

may be part of the problem.

Next slide, please.

Regarding training, we very much agree with the requirement for documented training on the requirements of Part 35.3045. That did lead to a number of issues that we've seen come up, and we feel that some additional training is definitely encouraged.

Annual training from a functional standpoint could be extremely difficult to carry out. There's a lot of time involved getting the physicians' time altogether, that's a large burden. So, I would suggest perhaps a two year interval after initial training to make sure everybody knows that perhaps consider a two-year interval. That is when other hospital credentialing, that's normal schedule for hospital credentialing, so we might tie it in with that.

Next slide, please.

Written directives. We agree that the establishment of a pre-implantation and post-implantation section of the written directive could help to clarify some of the issues that we've been having.

This is really getting to the concerns about real time planning versus preplans, which are still -- both of those are currently performed. So, having that divided could help with some of that.

We strongly enforce the need to be able to revise the written directive in the OR prior to the start of administration. I will make an additional comment on that on the next slide.

We would comment that 35.40(c)(2) should specifically state

that the oral revision must be performed prior to the start of any administration. It doesn't say that clearly right now and probably we think should clear that up.

Next slide, please.

I would call to your attention, though, a particular case. There is -- in discussing this with colleagues there is at least one instance where they receive a, based on an early ultrasound imaging of the prostate, they order loaded peripheral needles. So these are needles that they would insert in the patient that are preloaded with seeds, and the first thing they do is they implant those around the prostate.

After that, a plan is made for the internal seeds. They've already started implanting the seeds, so the administration has started. Then they do an additional further planning to get the dose distribution they want within the prostate.

This type of implant disallows a written directive being completed prior to the start of the case. So, this would very much change the practice of medicine at facilities that do it in this way, and that has to be taken into account. I'm not sure how to deal with that, but that is a reality.

And pre-implantation written directive for real time dosimetry implants should be based on dose, not activity. And the reason for this -- with respect to Dr. Hagan's comments -- when you're doing real time as we do it, we go in knowing what dose we want to give, 160 D90, then we make the plan to arrive at that dose.

And we may change that as we go through whether or not we

can get seeds in particular locations, various clinical realities force us to adjust the number of seeds that we put in and where we put them. We need the freedom to be able to do that, and if we had to specify exact activity that's going to be implanted, that could pose a burden, and again, get into regulating the practice of medicine. So we have to be careful with that.

I understand Dr. Hagan's comments, but it is another view on the world.

I certainly agree with Dr. Hagan's comments that we need to define dose much more precisely, it can't be just left open as dose. You're going to get it all over the place.

Medical events have certain meaning to them. And we've been debating about what medical event means. And there's one thing that has not been brought up, is that medical events bring about a congressional reporting, that medical events do go into a report that is taken to Congress. There is great weight put upon a medical event.

It's been roughly mentioned that it may be advisable to come up with something other than a medical event. If the intent is to capture something that hasn't gone according to plan but preserve that medical event for significant outcome, negative outcomes, establishing another category of something with information that you want to capture that doesn't have the weight of a medical event could be very beneficial and you could have much broader, more clinically realistic acceptance criteria for a medical event than perhaps 50 percent, which would allow for a lot of the medical realities once you're in the treatment room. But you would still be able to

capture the information that you want to capture.

The next slide, please.

Several questions that we have about the written directives. Does the NRC expect that the written directives will contain dose intent for other organs at risk such as the rectum, the bladder or urethra? We've talked about protecting normal tissue. Is it your intent to do that in an explicit manner? We are not commenting that you should or should not, but we would like clarification whether that's your intent.

And another question is, are the requirements of 35.41(d) met by the final treatment record in a real time dosimetry implant. As Dr. Hagan said, any dose is an estimate. What we're trying to do is get a handle on was this dose implanted properly.

If you'd go to the next slide, please.

This is an example that you're familiar with, I know you've seen this a number of times. The reason I bring it up here now is that this has within it information that's required to determine that the prostate or the implant has gone properly.

The prostate, urethra, the rectum and any other organs that a facility may wish are represented, the seed location are represented. This is done real time, I'm tracking the seeds during the implant, specifying where each seed has been implanted, as I see it, show up on the ultrasound.

There are studies that show that this type of -- the numbers from this analysis do correlate well with the CT dosimetry done at 30 days. So we want you to consider that.

Next slide, please.

Medical event reporting. We agree with the modification that the lack of a written directive in itself is not a, a medical event, and we strongly encourage you to, to maintain that unless there is insufficient information to determine if a medical event has otherwise happened.

We understand that you need to have some sort, something to hang your hat on, and this probably strikes a reasonable compromise on how to accomplish that.

Next slide, please.

I must commend you on having read an AAPM article and task group report, they are heavy reading. Congratulations for having made it through that.

CHAIRMAN JACZKO: I didn't say I made it through it.

MR. PFEIFFER: These are scientific articles, these are scientific publications. They have no intent in a regulatory framework, so we acknowledge that they should be used to inform the regulatory structure, but they are not intended to be, have text selected from them or be used explicitly in a regulatory format, and we thank you for keeping that in mind.

And finally, concluding remarks, if I could have my last slide, please.

In general, for the most part we agree with the re-proposed rules, and I said minor modification. I would probably, having reread my slides and other comments, I would strike the minor. There is some modification that's required to take in some of the other considerations.

But we are in general favor with the direction of it and we thank you for your consideration of our comments and those of other groups.

Thank you.

CHAIRMAN JACZKO: Thank you.

Dr. Davis.

DR. DAVIS: Thank you very much, Chairman and Commissioners for the opportunity to provide comments today. I'll do my best to try to finish this within the allotted seven minute timeframe.

My name is Brian Davis, I'm a radiation oncologist at the Mayo Clinic for the past twelve years and immediate past president of the American Brachytherapy Society, which is a 1,400 member organization consisting mostly of radiation oncologists and medical physicists, and arguably a medical society with more clinical experience in doing this procedure than any other, at least second to none.

At our institution we've done, in the past twelve years, approximately 1,000 of these procedures and I've published extensively on it.

I believe it is very important that the events of 2008 are looked at and that we want to make sure that these are not repeated, but how do we go about doing this?

I think that moving forward let me state very directly, without question, this rule in its current form intrudes on the practice of medicine and will work to limit access and negatively impact this procedure.

There are many practitioners that don't want bad press,

particularly when it is related to a clinically insignificant medical event.

Next slide, please.

What we really want to zero in on is the written directive where one needs to produce a dose that is plus or minus 20 percent what's in the written directive. And taking text from the revisions, the question is, can the authorized user revise the pre-implantation written directive after beginning the administration of brachytherapy. And here's where we have inserted an exclamation point and two question marks. No, this is not allowed.

This simply, the way brachytherapy is practiced and should be allowed to be practiced, won't work.

I don't believe that respected, experienced practitioners who have published widely on this procedure have been consulted in this particular aspect.

Next slide, please.

And in attempting to address this, it's stated however in 35.40(c) there allows for an existing written directive to be revised by an authorized user prior to beginning the administration in order to account for any changes in the treatment site. And in bold, that may have occurred between the time of planning the treatment and implantation procedure.

This is -- this -- these are often small changes, and this by itself does not address the true problem that the prostate changes size and shape during the implantation procedure itself.

Next slide, please.

Why is this wrong?

Volume change after permanent seed implant is unpredictable, so a dose determination at a single time point within 60 days can easily vary by more than what we consider in this particular rule an arbitrary 20 percent.

So if someone does a day zero CT scan and it's unacceptable, yet on day 30 it is acceptable, is this a medical event or not? According to the rules it's not clear.

This will result unquestionably in an over reporting of medical events which people understand is misadministration, without any justifiable clinical basis.

The RTOG, Radiation Therapy Oncologist Group, has conducted prospective clinical trials in prostate brachytherapy with certified centers. They have reviewed 400 cases from centers with experience in prostate brachytherapy and applied these rules to those 400 cases and found that 30 percent of them would be medical events.

You're going to shut down this procedure in a lot of places. It's not what your intent should be, but that's what will happen with this single rule.

If you want to add training, that's great.

We think the criteria with respect to reporting dosimetry within 60 days, that's long overdue, but this dose-based criteria is a problem.

Excellent long-term results reported for cases where intended dose prior to an implant varies by more than 20 percent after the implant, the

re-proposed rule amendments is delivering, ask this question, is a plus or minus 20 percent dose in permanent prostate brachytherapy routinely achievable? The answer is no.

Is it necessary? Looking at clinical results from centers with experience the answer is no.

Let's go to the next slide.

Let's see if we can activate this. This is a video, if you will, a graphic, of one way to do a seed implant.

Needles are typically placed from the anterior prostate to the posterior prostate. At training institutions, we often let residents place some of the initial needles. This is a needle eye view, if you will, the blue is the prostate. There's pelvic bones, the yellow is the urethra.

Putting in loose seeds, one by one, there is naturally some seed placement uncertainty that occurs and affects the ultimate dose. Also, if one uses loose seeds, which many institutions do, they can migrate in the veins. There's little clinical effect associated with that, but that is something that at our institution we attempt to avoid.

So part way through the procedure when the resident in training is doing it somewhat slowly and the operating room staffs want to move it along, that's when the attending staff takes over and we get the seeds in a timely manner. And it is considered acceptable to do dosimetry on the same day or to wait 30 days. The 60 days would seem perfectly reasonable.

You can compare a planned dose to a delivered dose. Where

you see that blue is where there's an area that is below the prescription dose. And that's something that occurs, and this is not accounting for edema. And I will tell you that it takes a lot of practice to get these prostates to rotate synchronously.

Let's move on to the next slide.

This is published data from our institution. We routinely take four prostate volumes. There's similar data published also from the University of California San Francisco which documents that the edema occurs and there is a great deal of unpredictability associated with it. The next slide, it's very important, this is in the peer reviewed medical literature, you will see what the ratio of the post-implant volume is to the pre-implant volume. If you pick any one of those bars, you'll see that there's a sizable percentage of prostate volumes that are outside plus or minus 20 percent. That's strongly related to dose.

The next slide shows our experience and what our D90's have been.

CHAIRMAN JACZKO: Can you define D90 for us.

DR. DAVIS: D90 is what the minimum dose to 90 percent of the prostate is. So 10 percent of the prostate can be get below that. You're allowed to have a cold spot. The D90 is much more, it is related in some series to clinical outcome and it's more reproducible.

CHAIRMAN JACZKO: And that's a more accepted, it's a more typical metric that's used.

DR. DAVIS: It is one of the metrics. The RTOG uses the D90

and something else known as the V100. It's not universally accepted, but it is something -- if someone wants to publish a paper on dosimetry, they ought to include D90 and V100.

CHAIRMAN JACZKO: And V100?

DR. DAVIS: V100 is the volume of the prostate that gets 100 percent of the dose.

Well, I ran overtime.

CHAIRMAN JACZKO: We'll forgive you.

DR. DAVIS: Okay.

Please go to the next slide.

We have combined our data from the last twelve yours with five other named institutions including Memorial Sloan-Kettering Cancer Center, Cleveland Clinic, University of California San Francisco, in one of the largest, if not the largest series of cases reported in the medical literature. Our dosimetry was typical of any in that group, if not better, and here is the variation.

In our practice we consider a D90 from 120 gray up to 200 gray something that is acceptable. Yet you see the percentage of cases that are above and below that. And the question is, did these patients all have a bad medical outcome, they're outside that range of even plus or minus 25 percent?

The answer is absolutely not.

Patients that are 10 years out that are in that lowest bin to the left, which have no detectable cancer and no side effects. Likewise at the

other end of the spectrum.

Last slide. This is the second to last slide.

This shows the results of prostate brachytherapy in terms of PSA control, one important metric in terms of outcome, compared to other procedures. The bottom one is external beam radiation therapy using doses which are lower than are typically used today, and this is prostate implantation with a variation of doses that we know occur in comparison to radical prostatectomy and higher dose external beam radiation therapy and showing equivalent outcome.

Next, concluding slide.

And please note that this has changed from some of the slides submitted earlier. I had the opportunity to review this with the chief radiation safety officer at the Mayo and other radiation physicists.

A dose-based regulation specified in the written directive prior to permanent implant will not work. I wish to strongly echo the comments of Dr. Hagan. It will lead to many clinically insignificant medical events.

An activity-based regulation is achievable, although that may have problems too.

A dose-based regulation will lead to centers stopping their permanent implant programs and will be a disservice to patient care in the United States.

CHAIRMAN JACZKO: Thank you.

Dr. Houchens.

DR. HOUCHENS: Thank you very much.

First slide, please.

I'm representing Us TOO International, it is the largest prostate cancer support education and advocacy groups in the country. I have spent 30 plus years in preclinical and clinical cancer research.

In 2001 I was diagnosed with prostate cancer and subsequently received an open radical prostatectomy and at later times hormonal ablation therapy and IMRT radiation, I have not had brachytherapy.

Next slide, please.

The mission of Us TOO is to communicate timely, personalized and reliable information and to enable informed choices regarding detection and treatment of prostate cancer.

Next slide.

You can see that we're quite large, we have over 325 chapters, mostly in the United States, but also in a number of overseas countries.

Next.

We work through support groups and these meet in medical institutions, hospitals, schools, churches, community organizations.

They offer peer to peer support, personal information sharing and information for partners and companions and families and also educational symposia and workshops.

Nest.

Through our central office support, the main office is in

Downers Grove, Illinois, we have a website which has newsletters and resource publications and materials for the people as well as patient referrals and chapter leader support.

Next.

This is a busy slide, but I wanted to show you some of the moderated bulletin boards that we have on the web covering a variety of areas related to prostate cancer.

You can see in the number two position up there is brachytherapy.

Next.

We also have a variety of educational programs, topic related teleconferences and webcasts, and we focus also on minority and underserved populations and have awareness programs and companion and family programs, as well as what is called Us TOO university, which are two-day workshops.

Next, please.

And through advocacy we work through a number of organizations, as well as attending conferences such as AUA and ASCO.

Next.

We have recommendations that focused on early detection, we believe it decreases deaths and improves the quality of life. And the benefits of early detection and treatment outweigh the cost and inconvenience of the occasional false positives.

Next.

You can see from this slide there is really a growing challenge. Currently there are about 230,000 cases a year diagnosed in the United States, and that is actually more than there are breast cancer patients diagnosed. But in the next 10 years we expect this number to go to about 300,000. So one in six baby boomer men will be diagnosed with prostate cancer, or about 6.6 million men are at risk.

Next.

We'll get into the areas of concern for patients. Clearly, probably the first one that comes up for men is will I be cured, or at least put into remission? And then the quality of life.

We all know that with prostate cancer most of the therapies do have side effects that range from minimal to very significant, such as impotence, incontinence, and a whole spectrum of other potential side effects.

The third point I have here is probably very important and relative to what's being discussed today, that is that knowledge of the doctors that have been chosen by the men, that they have the knowledge, that these have both the experience and the expertise in their field, whether that's urology, radiology, or medical oncology.

Now, I spoke recently to a physician who does a very large number of brachytherapy procedures a year to get his thoughts on this. And he said it is very common in his practice that when the patient is on the table under anesthesia that they most frequently, probably even up to 80 or 90 percent of the patients, make changes in the preplanning.

We've heard some of this from others today. But they use color flow doppler to determine possible more involvement. If they can find a tumor, extracapsular extension, involvement of seminal vessels, things that may not have been diagnosed or determined prior to that time.

This would throw most of these cases outside the 20 percent range that we're talking about because of the changes that they would make based on medical decision for using more radiation, more seeds, or placement in different locations.

We believe that it's the clinical judgment of the physician to make those decisions to give the best treatment to the patient for the possible cure.

In closing I would like to state that our organization would be happy to work through the NRC advisory committee patient rights advocate, Dr. Darryl Fisher, relating to issues that our organization has in regards to the use of medical isotopes.

Thank you very much.

CHAIRMAN JACZKO: Thank you, Dr. Houchens.

Commissioner Ostendorff.

COMMISSIONER OSTENDORFF: Thank you, Mr. Chairman.

I want to thank all the presenters for their very specific talking points and slides. I found it very helpful that with the things you agree with you kind of said yes, you agreed with the proposed rule, but where you had issues, you clearly stated those, and that was very helpful, so thank you.

I wanted to just kind of make sure, I'm looking at the different

parts of the proposed rule and along with my fellow Commissioner colleagues will have to look at this and make our own decisions. But I'm sensing there's a couple of things that I'm integrating from your comments or your lack of comments, that there is not really any concerns on the training requirements nor on the 60-day dose assessment piece.

Is that a fair conclusion I would draw from that? I couldn't tell. How about on the, you know, written directive, the absence of written directive and the lack of any other underlying information constituting a medical event, was that -- anyone want to comment on that? I was just trying to get a sense of where the community was.

Dr. Welsh.

DR. WELSH: Both the absence of a written directive and the 60-day requirement for post implant dosimetry, in the opinion of the subcommittee were events that don't directly have bearing on the health of the patients, and that's why we suggested if possible a regulatory event, rather than medical event. Because it needs to be underscored that the term "medical event," while in an ideal world is not of significance, in the real world it is of tremendous significance to a patient. And when a patient learns that a medical event has occurred, it sets off a chain reaction of medical/legal events that is very difficult to derail.

COMMISSIONER OSTENDORFF: Does anyone else want to comment on that aspect?

MR. PFEIFFER: I agree with Dr. Welsh's comment. I did say that we are generally in favor of not making the written directive itself, that there

should be some tracking of when appropriate information is not provided in a timely manner. And I would agree with Dr. Welsh's suggestion that putting this into a different category than a written or than a medical event is probably the right thing to do. And I implicitly included that when I was talking about having possibly two distinctions.

COMMISSIONER OSTENDORFF: Dr. Davis, I want to turn to one of your statements here on one of your slides, on your slide 12 and I want to make sure I understand.

I understand that you made a comment that a dose-based regulation will lead to curtailment or shutting down of procedures in X percent of the population. I don't know, I was kind of --

DR. DAVIS: I don't believe that anyone can predict that, but --

COMMISSIONER OSTENDORFF: But you believe it will have a deterrent effect in conducting procedures possibly or likely?

DR. DAVIS: If we could wager money on it, I would wager money on it.

COMMISSIONER OSTENDORFF: But your second bullet on slide 12 says an activity-based regulation is achievable.

Are you suggesting an activity-based regulation by itself with no dose limit is a proper way of looking at what you think from your position ought to go forward?

DR. DAVIS: The right now when we prescribe with permanent brachytherapy, we prescribe in millicuries. I'd also state what about in the situation where you -- in a different procedure where you use

radiopharmaceuticals, one injects iodine 131 that goes to a thyroid tumor. This would be similar to the situation where you have to say, tell us what that dose is using MERD dose calculations plus or minus 20 percent once you inject that radiopharmaceutical. That's just not going to happen. That is going to be very difficult to do.

So we have a seed implant where we're going to implant 80 seeds. We go into the operating room and check the prostate, fine, it's within 3 percent and we're going to use the preplan. The prostate starts to swell and we want to put in more seeds. It's rare that we would want to use, for example, more than 20 or 25 percent more than the 80 that we went into the operating room with. It is much more common in our institution and many other institutions in the RTOG that you're going to get plus or minus 20 percent in terms of dose.

It's easier to stay within the activity criteria if you're going to say that's what you're going to do when you go in the operating room than it is the dose criteria. But I still think the activity criteria by itself is a problem. It can still be a problem. And I could give examples of that, but it might take longer than the time we have.

COMMISSIONER OSTENDORFF: Does anyone else want to comment on Dr. Davis's answer there?

DR. HAGAN: Yes.

The activity-based metric has a lot going for it, but one problem that everyone recognizes is the distribution of seeds within the target volume.

There are published methods for dealing with that. And so sorting through how to sector the prostate to demonstrate that the distribution is within tolerance of the predicted or the intended distribution is certainly doable, and it doesn't force you to have to use an absorbed dose metric in order to make up for that flaw of an activity-based metric.

COMMISSIONER OSTENDORFF: Any other comments on that from the panel?

Any other comments on the discussion a couple minutes ago about, as I understand, the proposed rule in its current form possibly having a deterrent effect on the medical community being willing to administer the treatment?

Anyone also like to address that issue?

DR. DAVIS: I will make one statement.

Our organization, the American Brachytherapy Society, is holding a prostate brachytherapy school tomorrow in Chicago. We have over 150 attendees who do this every other year.

As chair of this meeting, this school, I went out to seek opinion, or get the best qualified speakers, the most widely published, experienced, so on and so forth. I know these people very well over the last 10 years.

I would be flabbergasted if you could get more than 20 percent of them to say that doing a dose-based criteria plus or minus 20 percent is something that they do all the time and is reasonable to impose on the community.

COMMISSIONER OSTENDORFF: Dr. Houchens, from the advocacy educational perspective, in your prior experience do you have any comments on the impact this proposed rule might have on the patient community?

DR. HOUCHENS: Certainly the patient's first concern is I want to get well. But, clearly, as I pointed out, they want to do that through the best doctors they can find. And I think if the doctors were strapped with having to spend more time on paperwork and reporting changes in plans and so forth, that could limit what can be done.

COMMISSIONER OSTENDORFF: Yes, Dr. Welsh.

DR. WELSH: I alluded to this point in my presentation that we would not want to see overly restrictive regulation to result in this particular modality fading and becoming unavailable to patients who could benefit.

And I do fear that if many of the procedures become labeled as medical events, even if we decide here that medical event doesn't mean that much, patients are going to hear X percentage of people who undergo prostate brachytherapy have medical events. They're not going to understand what we're talking about and they're going to shy away from this procedure, which in fact, is perhaps the safest of the -- and certainly the most convenient of the three modalities for treating prostate cancer.

In comparison to surgery, for example, there is the additional layer of complexity imposed by NRC regulation that makes this the safest and most -- the safest of the procedures that is available.

But it's a fine line between assurance that regulation is

appropriate and maintain safety for the patient versus scaring parents away. And I do fear that if some of the predictions that there could be thousands of medical events with the new re-proposed rules, this would certainly deter practitioners from offering it and deter patients from seeking it.

COMMISSIONER OSTENDORFF: Thank you.

Thank you, Mr. Chairman.

CHAIRMAN JACZKO: Commissioner Svinicki.

COMMISSIONER SVINICKI: I want to thank you all for agreeing to appear here today, I know you have other demands in the medical context on your time, so I appreciate your contribution on these issues.

Dr. Welsh, please convey to the members of your subcommittee and the ACMUI as a whole again I'm very appreciative of their contributions to these medical issues to the NRC staff and for the opportunities where they interact with the Commission. I benefit a lot from their views.

Just some specific questions. I think we've covered a lot of very valuable territory and Commissioner Ostendorff covered a number of issues as well.

But, Dr. Welsh, your proposal that was touched upon of the V(init), is that something that has been discussed in more detail with the NRC staff or is that at a more conceptual stage?

DR. WELSH: It is at a more conceptual stage right now.

Part of the difficulty that the ACMUI and the subcommittee in particular has faced is that the re-proposed rule became available to some members after the subcommittee report was due and, therefore, the original

subcommittee report that was discussed with staff at the ACMUI meeting in May differs substantially from the latest version of the subcommittee report, which counts for and includes all of the re-proposed rule that has been made available.

COMMISSIONER SVINICKI: I made some reference with the first staff panel to the fact that ACMUI, perhaps your subcommittee, had under development of a report or comment document on the re-proposed rule.

Again, I've that as kind of a folklore. is that accurate?

DR. WELSH: The subcommittee has formulated an official report, it has been submitted. And the subcommittee has been reluctant to put into words any proposed rule without discussing it with stakeholders for fear that it could be misconstrued as something coming directly from the stakeholders and difficult to erase once it is put in writing. But I can say that the ACMUI subcommittee has formulated some proposed rules that could be offered in writing.

COMMISSIONER SVINICKI: Is that something -- if the Commission were to approve publication of the re-proposed rule in its current form, is the work that you're describing now in the comment development or perhaps proposed regulatory language itself, is that something you would submit in a comment period, then, is that how you would go about pursuing that?

DR. WELSH: If that is the only alternative, yes, of course.

COMMISSIONER SVINICKI: Okay. Is there other -- okay. So you said if that's the only alternative.

And I'm not, again, acquainted with the frequency of your

subcommittee meeting schedule or the ACMUI as a whole. Would there -- is there a regularized engagement with the staff, would you have anything planned in the coming months?

DR. WELSH: We don't have anything scheduled.

COMMISSIONER SVINICKI: Okay. Thank you.

Dr. Houchens, I would -- and again, Dr. Welsh has commented on this a couple of times, of the reaction of patients and their families to a medical event and not really understanding, and again, that strong correlation that a patient or their family is likely to make with an adverse health outcome with the term "medical event."

Is there anything that you would like to add to that in terms of education campaigns or other things?

DR. HOUCHENS: Well, I think certainly through education, clearly cancer patients, not just prostate cancer, but any patients are very shaky and very concerned, as their families are, in having treatment and getting it taken care of and in doing it well.

So I think there would be the perception that if they heard there was a medical event and they would want to know, well, what is that, what does that mean.

It would be difficult to explain to the average person, I think, the average patient, what exactly was entailed there, that this doesn't mean there was an error, but that there was something that had to be, needed to be reported.

They don't want to be burdened with those kind of things,

obviously.

And so I think, again, through, it's possible through some education it could be done, but it would be difficult in every chapter, in every location we have to have the right people to give them the answers and definitions on that, I think.

COMMISSIONER SVINICKI: And, again, just going on the terminology, it's hard for me as a layperson to think of how I would explain to somebody that it's significant enough that it must be reported, and yet it's not significant -- may or may not be significant to your health. So I think that that would be difficult to have them really understand or perhaps even believe that that's the case. I think there would be a real challenge there in doing that education.

And then, finally, again, I thank all of you for your presentation. But is there anything that you heard in response, that the staff gave in response to the Commission's questions in the first panel. I would offer any of you an opportunity if there's anything you'd like to give a perspective on, if you heard the NRC staff respond to a question and you would like to state anything in addition to that.

I'm not seeing anyone very eagerly jump up so ...

Yes, Dr. Davis.

DR. DAVIS: I believe that the stakeholders and the individuals in this country that have a lot of experience doing this procedure need to be canvassed a lot more closely.

I think it would also be a bad idea to put forward re-proposed

rules that once again have the dose-based criteria when this is really more canvassing of people with experience in this procedure has apparently not been done, at least from my perspective.

COMMISSIONER SVINICKI: Okay. Thank you.

Mr. Pfeiffer.

MR. PFEIFFER: Thank you, Commissioner.

A couple of things.

And this is a point of clarification, and I don't have the rule -- the as yet not quite re-proposed rule in front of me. But my understanding is that it allows for dose-based criteria but it does not require it.

And if anybody can clarify that. I understand that there are concerns about that.

CHAIRMAN JACZKO: Can you clarify that point?

MR. PFEIFFER: That facilities can use activity-based strictly under the current form of this. I just wanted that clarified.

CHAIRMAN JACZKO: We have a staffer here that can.

MR. LOHR: If I may. The re-proposed rule has dose requirements as well as activity-based requirements.

CHAIRMAN JACZKO: Both, it's not an either/or, it's both.

MR. LOHR: That is correct.

MR. PFEIFFER: Then I would encourage a revision on that to allow one of the other, depending on local practice, and that may help clear up some of these other concerns.

And at one staff point one of the staff members did state that

it's best to have the events reported, that -- and this gets back to what we've been talking about, having a way to report without having to tell the patient about it, and reporting to the doctor, reporting to all of those other people. There needs to be a more subtle way to let NRC collect the data to know that something didn't quite work right, but without all of the other baggage associated with it.

COMMISSIONER SVINICKI: Thank you.

Dr. Hagan, did you have a comment?

DR. HAGAN: Yes.

One of the comments made by Jim Luehman was that the, the proposed move to an activity-based metric was derailed by events at Philadelphia, and the underlying assumption was that the evaluation that produced through absorbed dose metric determination a high number of medical events reported out of Philadelphia was correct, and that when an activity-based metric was applied and the number was much lower, than the feeling was, well, you'd lost some legitimate medical events, and I don't believe that's the case.

I think the correct posture is that the evaluation that led to those very high numbers in Philadelphia was flawed. And that an appropriate one using V(init) or using activity-based metric provides the same subset of that population, which may have removed or reduced the pressure to move to a dose-based metric.

COMMISSIONER SVINICKI: Thank you.

And Dr. Welsh, did you have anything?

DR. WELSH: This is in reference to one of the comments by Dr. Zelac, who pointed out that there can be volume changes, volume increases, which would alter dosimetry if done early, but be rectified if done at a later date. This is true.

And in an ideal world we would do post implant dosimetry perhaps multiple times to get a curve that truly depicts total dose. So dose at any instant is a function of volume which is a function of time, and it's a function of radioactive decay, which is also a function of time.

But this process of getting a later post-implant dosimetry point works for edema, but it does not work for shrinkage. So shrinkage and edema are what I call anatomic volume changes. These anatomic volume changes in my opinion should be categorized as patient factors because they are beyond the authorized user's control and, perhaps, should not be considered medical events if dose deviates because of this patient-related phenomenon.

COMMISSIONER SVINICKI: Thank you.

Thank you, Mr. Chairman.

CHAIRMAN JACZKO: Commissioner Magwood.

COMMISSIONER MAGWOOD: Thank you, Mr. Chairman.

I thank all of you for appearing today. It's been a very educational discussion this morning or this afternoon. The day's gone by fast.

Dr. Davis, I was going through your presentation and I noted you had highlighted a section from the rule, and you'll be happy to know that

I didn't use exclamation points, but I highlighted it in red because it leapt out at me.

This is the section of the rule that asks the question, can the authorized user advise pre-implementation written directive after beginning the administration of brachytherapy and the answer is no, you cannot change it once it starts.

And we did hear that there is some flexibility about, you know, when you can change it before it starts, but it was pretty clear that that wasn't sufficient in your view. And I wonder if you could elaborate on that a little bit and I can discuss that with you.

DR. DAVIS: Let me give you one example.

There was a patient treated at another medical center about 100 miles away from the Mayo Clinic eight years ago. People with less experience started the procedure, and as they progressed they were able to implant six seeds of approximately a planned 80 and then determined that the pubic arch was in the way and they couldn't complete the procedure, so they stopped. And I think that that was the right thing to do.

Was that a medical event?

You know, that is something for different individuals to define, but they did the right thing. The patient came to our institution for a second opinion. We did an implant two months later, discounting the effect of those six seeds.

Was this patient mistreated grossly?

I don't think so.

I think that the doctors were mature in saying we can't do this, we're going to stop.

Under the current requirements, they are not required to report that as a misadministration. If they were, and this gets publicized, one article in a local newspaper really kind of ruins a program and ruins your day, particularly when the person writing it, you know, doesn't necessarily know a lot about it.

And that's not something that's happened at our institution, but that's one example of what can happen.

Another is a patient could have a dose, say they want a dose of 145 gray and when they finish the does it's 110 gray, or let's say 25 percent below what you want, you can then often treat that patient with supplemental external beam radiation therapy, which is often done as a planned approach.

This patient is not mistreated, other than the fact that they may have been informed we're going to be able to do this with an implant and now you need to get an implant plus external beam radiation therapy.

I'm not sure that, you know, this is something that you want to publicize.

Is this something that is common in our practice? No, but as a representative of an organization that encompasses a lot of different practices, I think that you're trying to force, I don't know, a square peg in a round hole because of many of the factors that other speakers have outlined of things that can change in the operating room.

COMMISSIONER MAGWOOD: Can you describe what you think the appropriate procedure for a written directive would be?

DR. DAVIS: I think that you -- there is a blue ribbon panel that is working on certain constraints.

I think if you take everything that's been done and remove the dose constraint, instead of enforcing that, say we're going to collect that data from the NRC over several yours, and then reevaluate it.

But what an important written directive is is that we are going to implant a certain amount of activity. We sign our written directives after the procedure is done and that this was in the prostate.

The real harm comes when poor imaging of the prostate happens and seeds, a big group of seeds are implanted in adjacent structures where you can cause harm. That's where the big problem comes in.

It happens much less frequently than the current regulations would identify what a misadministration or medical event would be.

I'm trying to answer your question, maybe not as in-depth as it needs to be.

COMMISSIONER MAGWOOD: I think you answered the question.

I've read this in several documents and articles I've look at over this and it's clear that there are people in the medical community who believe that the post application written directive is the appropriate path to take.

But, you know, of course you have your problems, we have our problems. And one immediate issue that raises from a regulatory standpoint is how can we, how can we as a regulator hold the authorized users -- let's not call them doctors for the moment, let's call them authorized users -- to what they said they were going to do if what they said they were going to do is created after the fact? How to we deal with that?

DR. DAVIS: Well, there is another group of individuals, radiation oncologists, with extensive experience in prostate brachytherapy, a blue ribbon panel, that I've talked to some of the members of the panel.

One is a criteria that looks at how much dose was given to important structures more than a centimeter away from the prostate, was it more than one cc of a structure, more than one centimeter away get greater than 150 percent of the prescribed dose as something that indicates that you're doing your implants wrong.

I mean really, to me, that needs to be the question, and perhaps as regulators you're compelled to come up with a solution. But as a physician we try to do things or at least that are in the best interest of the patient, and the government will want you to do things that are in the best interest of patients too, in medical practice.

COMMISSIONER MAGWOOD: So from what -- based on that, then what you're saying is that the criteria, the written directive the whole structure really is, in your view, not the right approach to take to looking at this; that we ought to be looking at the outcomes at the end and measuring unintended doses, is that in effect what you're --

DR. DAVIS: Well, I think unintended doses outside of the target volume, which includes the prostate and whatever the clinician wants to define, and then pose that question to, for example, the radiation therapy oncology group database, which is a National Cancer Institute funded clinical trial organization, it's one of the biggest six in the country. That group has gone through a significant vetting process in how do we run a clinical trial for prostate brachytherapy, how do we measure when an implant is acceptable or not.

By this criteria they say there's going to be 30 percent medical events from experienced medical institutions in prostate brachytherapy based on these 400 cases.

I'm not sure that's what anyone at this table or in this room wants to see happen with the next 400 patients that are on clinical trial.

COMMISSIONER MAGWOOD: You mentioned in your last response the treatment site.

What is a treatment site and how do you define it?

DR. DAVIS: Well, it is the prostate. Patients undergo prostatectomy 30 to 80 percent of the time based on older pathologic data have multi-focal disease, so the entire prostate is generally the target. But then there's a margin that's incorporated to cover extra-prostatic extension and also uncertainty in imaging, whether it's ultrasound or CT. And there are areas around the prostate where you can, you can treat with radiation and it's of little consequence for example, laterally and anteriorly, but posteriorly where the rectum is, that's a critical structure where the most feared side effect really can occur.

So it is the prostate plus a margin around it, and the RTOG uses five millimeters around the entire prostate except zero millimeters posterior. So that's the target volume.

So you can put seeds outside of the prostate, but it's still treating prostate cancer in and around the prostate.

COMMISSIONER MAGWOOD: So your concept of what the treatment site is compatible with the planning volume that we've heard about from others?

DR. DAVIS: Yes, planning volume is one terminology, yes.

COMMISSIONER MAGWOOD: Okay. I still have a minute and a half, but I don't have any more questions. Does anyone want to weigh in on anything that was said, please.

DR. HAGAN: Yeah, let me weigh in on that last point.

We asked that specific question to the blue ribbon panel that the VA convened, because definition of the treatment site for an activity metric is quite important. And, in fact, if it's possible to go back to my slides, there's an additional slide at the end of the slides, the sixth slide, that shows exactly the issue that Brian was just talking about.

And that's -- their conclusion was the treatment site was that volume in which the authorized user intended to implant seeds in order to treat the prostate whether the authorized user was intending to treat the prostate alone or the prostate plus a margin outside. Based on different styles from practitioner to practitioner, the desire to put seeds outside of the prostate varies. And, in fact, if there's any chance --

What that slide would show is that two of our very well known practitioners, one places, attempts to place essentially all the seeds within the prostate volume and very few seeds are placed -- this is the slide.

So at the top there's an implant that comes from Cincinnati where their rubric is to place seeds largely within the prostate, and this shows a preplan and a post plan that looks very, very nice, the seeds are pretty much exactly where they were planned. And then below it is an implant from Puget Sound where the desire is to place most of the seeds or many of the seeds outside the prostate using a higher activity, and it then becomes, the dose becomes less sensitive to the volume changes and you can do a much more robust dose analysis early on because of that. You wind up dosing additional tissues a little more, but you wind up having a much more uniform dose throughout the prostate volume.

So those are style differences that change the treatment site from the prostate to the prostate plus a ten millimeter margin in the case of the style of a different practitioner. So the need to definition -- to provide a definition of treatment site needs to be flexible, it needs to be able to apply to practitioners of each end of that style spectrum.

COMMISSIONER MAGWOOD: Thank all of you very much. Thank you Mr. Chairman.

CHAIRMAN JACZKO: Well, thank you. I appreciate your last comment, Dr. Hagan.

I think certainly, you know, sometimes that we get a little bit lost in some of the issues, but I think the intent of the staff, and again we may have a

different disagreement among different members here. I think Dr. Welsh said there's a strong interest from ACMUI to define treatment site. I think the staff left the term treatment site in the rule to provide that flexibility rather than going with a specific definition.

So I think there was an attempt for the staff to be flexible, it sounds like that's an approach that you would be more comfortable with.

I want to make one comment. I think there was a mention, I don't know remember who made it, that medical events are reported to Congress. That's not an accurate statement.

MR. PFEIFFER: I said that.

CHAIRMAN JACZKO: Okay. Thank you. Because we report abnormal occurrences, sometimes they involve medical events, but they, in fact, involve violations of our regulations that are of clinical or health and safety significance. So it doesn't rise to that level, certainly, of reporting.

The other point I would make, and this has been a very interesting discussion, and I certainly appreciated the feedback and the comments. One comment I'll make, I think as Commissioner Magwood said, you have your problems and we have ours.

We don't use activity. Activity is an irrelevant concept in many ways for us. We care about dose. That's because we're a public health and safety regulator.

Activity is a physical measure of amount of times an atom will undergo fission reaction. That has nothing to do with dose.

I mean, you know, we have a similar situation right now in the

State of Vermont and I'm actually going up there next week to, to try and explain some of these differences, because we have tritium in water in Vermont.

Tritium in water is irrelevant from a public health and safety standpoint if nobody's drinking the water. That activity can be 10 million picocuries per liter, which is several times above the public established limits, but it becomes an issue when it becomes a dose, when it becomes ingested into the body and then that water goes to various organs and emits radiation to the tissue and creates a dose.

So in some way shape or form across the metric has to the dose. I mean talking about activity really gives us no insight into what the impact is from a public health and safety standpoint.

So, you know, I'm pleased, I think at the end, what I heard, and quite frankly seemed to be more discussion about dose. And that, you know. as we go forward, that the focus for us needs to be to think about the right ways to capture the dose, maybe 20 percent is not the right variance with this particular procedure given the difficulties in estimating the doses here.

It seems that the uncertainties in the dose calculations are probably greater than 20 percent, I mean that's basically the problem that we're dealing with.

So the medical event definition is getting into what -- we're not in the precision of the calculations themselves. Maybe it's 40 percent, maybe it's 50 percent, maybe there's additional ways to determine what the volume is, as Dr. Welsh said.

But when I hear certainly from my perspective, that the activity

concept, it just doesn't register with me because it's not about what we're interested in, which is ultimately what the impact of the radiation is on the tissue, which is the dose. And that's what we're talking about.

So, it certainly seems like there are a lot of interesting suggestions, and maybe there is more, more that we need to do.

We are certainly at that stage where I think what the commission has in front of us is reexamining whether or not to even publish a proposed rule. I mean certainly in my opinion it's worth putting out a proposed rule, because I think clearly we'd agree that the current definition is perhaps not one that is working, so we need some new ideas and new concepts.

But from my perspective an activity-based definition doesn't help. It doesn't satisfy I think what we need to satisfy from our perspective, but I recognize that there are challenges developing a dose criteria. But I think that's the issue we have in front of us is to figure out how best to do that in a way that, that doesn't prevent a clinically successful practice from occurring.

And, I think as the Commission continues to look at this, I hope that's the spirit in which we'll look at this, that it clearly, I think the best thing we can do is put down a definition, get comments and feedback on that, and I think in particular Dr. Davis, you've given us some good places that we want to make sure that we capture.

I think some of the these, the blue ribbon -- I think you talked there's a blue ribbon panel you created or that there is a, or at least a subgroup of your organization that we could go to that could help solicit comments on an, on an acceptable way for us to find some reporting in this area, but certainly we

can follow-up if there's a specific contact as we go forward to ensure that we're getting those comments and feedback. But that's certainly my perspective.

I don't really have any other questions at this point. I think my colleagues have offered some, some very good questions, and certainly at this point I'll turn to my colleagues if they have closing comments as we go forward.

COMMISSIONER OSTENDORFF: I found this very helpful, I learned a lot and I think it would be helpful in the SRM to ask the staff to provide some feedback from what we've heard from this panel on some specific issues, one of those dealing with the notion that Dr. Welsh raised, and I think Dr. Hagan had supported, about normalizing the organ volume. I'd like to hear what the staff has to say about that and to what extent that has been considered. They may have, and I'm not aware of that. So I'd suggest we ought to have that be part of the SRN.

I know Commissioner Svinicki had raised the issue about at what point in time we might receive some feedback from the advisory committee on some of these issues and whether it's done as part of -- if the rule is going to go out as a proposed rule, is it done as part of that process or is there a separate, a more near term feedback option? So, option review, how we might explore that second piece as well.

CHAIRMAN JACZKO: I appreciate that.

I don't know if others have comments.

Certainly Commissioner Magwood would support that. Certainly on the first point I think it's a very intriguing idea. It seems that the volume is the issue here, understanding the volume and understanding the

volume changes over time as the dose does, and the volume is not -- dose is a fairly easy -- the time dependence of dose is a fairly easy thing to calculate if you know the radionuclide constituents. But the volume seems to be a bit more of a challenge here. It seems like a very intriguing idea.

And the other point we can check on the process for ACMUI comment response, but I think those are two very good things to look at in the SRM.

Any other comments?

Well, again, I want to thank everyone for sharing your insights on this very important and, and complicated issue.

Thanks.

(Whereupon the proceedings were concluded)

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