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NUCLEAR REGULATORY COMMISSION

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ADVISORY COMMITTEE ON MEDICAL USES OF ISOTOPES

+ + + + +

Tuesday, January 18, 2005

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Telephone Conference Call

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The above-entitled matter came on for hearing, pursuant to notice, at 1:00 p.m, Leon S. Malmud, M.D., Chair, presiding.

COMMITTEE MEMBERS PRESENT:

LEON S. MALMUD, M.D. Chair

JEFFREY F. WILLIAMSON, Ph.D., Member

DOUGLAS F. EGGLI, M.D., Member

RALPH P. LIETO, Member

SUBIR NAG, M.D., Member

SALLY SCHWARZ, R.Ph., Member

ORHAN SULEIMAN, Ph.D., Member

RICHARD J. VETTER, Ph.D., Member

NRC STAFF PRESENT:

THOMAS H. ESSIG, Designated Federal Official

IVELISSE CABRERA

CYNTHIA FLANNERY

LINDA GERSEY

AARON McCRAW

ANGELA McINTOSH

RONALD ZELAC, Ph.D.

ALSO PRESENT:

LISA DIMMICK, Nucletron Corporation

ROSHUNDA DRUMMOND, American Association for Therapeutic Radiology and Oncology

LYNNE FAIROBENT, American College of Radiology

MELISSA MARTIN, American College of Radiology

GLORIA ROMANELLI, American College of Radiology

I-N-D-E-X

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

1:10 p.m.

MR. ESSIG: On the record. All right. I would like to open the meeting as Designated Federal Official. I am pleased to welcome you to this publicly noticed conference call meeting of the ACMUI. My name is Thomas Essig. I'm Branch Chief of the Material Safety Inspection Branch and I've been designated as a Federal Official for this advisory committee in accordance with 10 CFR Part 7.11.

This is an announced meeting of the Committee being held in accordance with the rules and regulations of the Federal Advisory Committee Act and the Nuclear Regulatory Commission. The meeting was announced in the December 22, 2004 edition of the Federal Register. Today's meeting will focus on an update of the criteria for definition of a medical event. An ACMUI subcommittee has been reviewing this area and will share its recommendations with the full Committee today.

The function of the Committee is to advise the staff on issues and questions that arise on the medical use of byproduct material. The Committee provides counsel for the staff but does not determine or direct the actual decisions of the staff or the

Commission. The NRC solicits the views of the Committee and values them very much.

A request that whenever possible we try to reach consensus on the various issues that we will discuss during this conference call, but I also value minority or dissenting opinions. If you have such opinions, please allow them to be read into the record.

As part of the preparation for this meeting, I have reviewed the agenda for members and employment interests based on the general nature of the discussion we're going to have today. I've not identified any items that would pose a conflict. Therefore, I see no need for individual members of the Committee to recuse themselves from the Committee's decisions making activities. However, if during the course of our business you determine that you have some conflict, please state it for the record and recuse yourself from that particular aspect of the discussion.

At this point, I would like to perform a roll call of members that may be participating today. Healthcare Administrator and Chairman Dr. Leon Malmud. I think we recognize that he'll be a little bit late. State Representative Mr. Edgar Bailey. Nuclear

Medicine Physician, Dr. Douglas Eggli.

DR. EGGLI: I'm here.

MR. ESSIG: Okay. Radiation Oncologist Dr. David Diamond. Radiation Oncologist Dr. Subir Nag.

DR. NAG: Yes, I'm here.

MR. ESSIG: Nuclear Pharmacist Ms. Sally Schwarz.

CHAIRMAN MALMUD: Leon Malmud.

MR. ESSIG: Ah, excellent. I just called your name and you are now here. Good. This is Tom Essig, Dr. Malmud. I'm just going through my opening remarks and I was about ready to turn it over to you or chair the opening part of the meeting myself. But now that you're here, I'll turn it over to you as soon as I'm done with these remarks.

CHAIRMAN MALMUD: Thank you.

MR. ESSIG: Radiation and Safety Officer Dr. Richard Vetter.

DR. VETTER: Here.

MR. ESSIG: Therapy Physicist Dr. Jeffrey Williamson.

DR. WILLIAMSON: Here.

MR. ESSIG: Nuclear Medicine Physicist Mr. Ralph Lieto.

MR. LIETO: Present.

MR. ESSIG: Okay. Patient Advocate Representative Dr. Robert Schenter. Nuclear Cardiologist Dr. William van Decker. Representative of the Center for Devices in Radiological Health Dr. Orhan Suleiman.

DR. SULEIMAN: Present.

MR. ESSIG: Okay. And let me just do a quick count here. Seven. Mr. Chairman, we barely have a quorum, but we do. I know ask NRC staff who are present to identify themselves. I'll start with the individuals in the room here and then we'll turn it over to others of NRC who may be calling in from elsewhere.

MS. CABRERA: Ivelisse Cabrera.

DR. ZELAC: Dr. Ronald Zelac.

MR. McCRAW: Aaron McCraw.

MS. GERSEY: Linda Gersey.

MR. ESSIG: Okay. Others from NRC who are calling in remotely.

MS. FLANNERY: Cindy Flannery.

MR. ESSIG: Okay. Anybody else from NRC? I would ask members of the public who are participating if they wish to identify themselves, please.

MS. FAIROBENT: Lynne Fairobent, ACR.

MS. DIMMICK: Lisa Dimmick, Nucletron Corporation.

MS. MARTIN: This is Melissa Martin with ACR.

MS. DRUMMOND: Roshunda Drummond with AATRO.

MS. ROMANELLI: Gloria Romanelli, ACR.

MR. ESSIG: Okay. Following the discussion of each item, the Chair at his option may entertain comments or questions from the members of the public who are participating with us today. At this point, Dr. Malmud, I would turn the meeting over to you.

CHAIRMAN MALMUD: Tom, could you just keep it going? I have a problem here. I'm on the line but just get it going.

MR. ESSIG: Sure. Will do.

CHAIRMAN MALMUD: Thank you.

MR. ESSIG: Okay. I believe that from what I said earlier, the purpose of today's meeting is to hear for the full Committee the recommendation from the Medical Event Subcommittee on the certain criteria associated with the definition of a medical event. So I would turn to the Subcommittee Chair and we'll start

the discussion there and then Dr. Malmud will join us as he can.

CHAIRMAN MALMUD: I'm here, but I -- Go ahead.

MR. ESSIG: Okay. Subcommittee Chair.

DR. WILLIAMSON: Okay. This is Jeff Williamson. I hope all of the members of the ACMUI and the NRC staff have a copy of the revised report that I sent out early this morning, January 18th. What I will do is maybe make a few introductory remarks to explain the process we went through and then simply step through the different recommendations in the report for ACMUI discussion. Would that be appropriate, Tom?

CHAIRMAN MALMUD: Yes, Jeff. Thank you.

DR. WILLIAMSON: Oh, you're here now, Leon. Okay, I didn't realize. All right. Well, this task was assigned to the ad hoc subcommittee on medical events at the ACMUI meeting of October 18, 2004. We were asked to address problems in the medical event report criterion specifically focusing on permanent brachytherapy implants. This issue was raised originally by Dr. Nag at our last briefing with the NRC Commissioners. The NRC Commissioners responded with a staff requirement memo asking the

staff with ACMUI advice (a) to evaluate the appropriateness and justification of the 20 percent threshold currently built into the Medical Event Reporting Rule and (b) consider appropriate ways for conveying risk, if any, associated with these levels of discrepancy.

So to develop some recommendations in this highly controversial and very technically complicated area, the Subcommittee met twice, once on December 7, 2004 and more recently, on January 13th, I believe, in a non-public telephone conference call. So the lateness of this last meeting or proximity to this meeting is the reason why revised recommendations were not available on a more timely basis. Are questions about our charge and the process by which we develop the recommendations?

CHAIRMAN MALMUD: This is Malmud. No questions about the charge. Are there questions from other members of the Committee to Dr. Williamson? If not, please move ahead.

DR. WILLIAMSON: Okay, well let me before I jump in, I want to acknowledge the important role played by the Subcommittee members who were Dr. David Diamond, Mr. Ralph Lieto, Mr. Subir Nag in addition to myself. I think this was very much a team effort.

So with that introduction, I would like to start with the document. The document is divided into important issues that we considered and then under each issue, there are some recommendations that were made which are indicated in bold type.

I think to make the flow of this most logical what I would like to do is start with issue number two and then after we've dealt with two through four, maybe come back and pick up number one if the Subcommittee agrees that's appropriate. I think some of the issues depend on one another and it would be helpful to get some consensus on the technical points first.

CHAIRMAN MALMUD: Thank you, Jeff. Is everyone agreeable to doing two first?

DR. NAG: Yes.

CHAIRMAN MALMUD: Thank you.

DR. WILLIAMSON: So the issue number two can be stated as follows: "Is the 20 percent absorbed dose threshold a reasonable reporting criterion for over and under doses to the target volume?" And this is specifically for permanent seed implant although there are some comments for other types of radiation medicine procedures as well.

So in general, the Subcommittee rejected

the concept of replacing a single prescribed dose with a dose range. This is absorbed dose now that we're talking about for brachytherapy implants on the basis that this is inconsistent with the current mainstream industry practices whereby a prescribed dose is specified in terms of a single well-defined value rather than a range. So we really didn't consider that further. I guess you could take that as a recommendation.

Maybe it would be helpful if I read the recommendations under this part and then we can decide what to do. The first recommendation is that "20 percent is a reasonable action level for reporting events of QA significance to NRC for temporary implants, external beam treatments and unsealed radiopharmaceutical administrations." Are there comments on that and specifically from our Chairman, do you want to entertain votes on these piece by piece or do you want to hear the whole thing?

CHAIRMAN MALMUD: I think it would be more efficient if we did it piece by piece.

DR. WILLIAMSON: Okay.

CHAIRMAN MALMUD: Is there agreement among the Committee to do it piece by piece?

DR. VETTER: Yes.

CHAIRMAN MALMUD: Thank you.

MR. LIETO: Yes.

CHAIRMAN MALMUD: Thank you. All right. So, Jeff, what's the first piece?

DR. WILLIAMSON: The motion is that in concordance with Dr. Siegel's assessment and past ACMUI discussion the motion is 20 percent is a reasonable action level for reporting events of QA significance to NRC for temporary implants, external beam treatments and unsealed radiopharmaceutical administration.

CHAIRMAN MALMUD: Is there a second to the motion?

MR. LIETO: Second. This is Ralph Lieto.

CHAIRMAN MALMUD: Thank you, Ralph. Is there any discussion of the motion?

DR. VETTER: This is Dick Vetter. I have a question.

CHAIRMAN MALMUD: Yes.

DR. VETTER: This motion seems to go beyond the charge of the Committee in that it recommends including (Beep sound) radiopharmaceutical administrations. Since those were not addressed here by this subcommittee specifically, I'm wondering whether the motion shouldn't be limited to temporary

implants.

CHAIRMAN MALMUD: Is there anyone else who agrees with that observation?

DR. NAG: I agree with Dick.

CHAIRMAN MALMUD: All right.

MR. LIETO: I -- This is Ralph Lieto. I do not.

CHAIRMAN MALMUD: Don't agree with Dick?

MR. LIETO: No, I think it's within the charge if you will in the March 16, 2004 notice from the Commissioners as to what the question was that we were supposed to address. It mentioned all modalities.

DR. WILLIAMSON: This is Jeff Williamson. As having tried to dig out from the transcript of October 16 I believe what exactly our charge was, it's not especially clear that it was limited exclusively to permanent implants although that's certainly what we emphasized in the majority of our discussions.

DR. ZELAC: Dr. Malmud.

CHAIRMAN MALMUD: Yes. Who is this?

DR. ZELAC: This is Dr. Zelac.

CHAIRMAN MALMUD: Yes, Ron.

DR. ZELAC: I just wanted to put in a little historical perspective on this. At the October

meeting of the Advisory Committee, this question was considered and the various modalities for which the plus or minus 20 percent might be appropriate based on the information from Dr. Siegel that I had provided was considered.

The decision at that meeting of the Advisory Committee was that the plus or minus 20 percent was an appropriate criterion of all modalities with the possible exception of permanent implant brachytherapy and it was on that basis that the subcommittee was formed to consider that specific modality. However, this recommendation from the Subcommittee is in line with the earlier vote and decision by the whole Committee that the plus or minus 20 percent was in fact an appropriate criterion for all the other modalities.

CHAIRMAN MALMUD: Thank you, Dr. Zelac. Dr. Vetter, would you care to comment?

DR. VETTER: I did. I'm satisfied with that explanation.

CHAIRMAN MALMUD: Thank you. With that explanation, do we accept Dr. Williamson's motion as presented.

DR. NAG: But I think that motion is repeating because that has already been accepted

before by the whole Committee and it was only the permanent implants that was in question. So, yes, we have that motion, but this has already been voted on and has been accepted. We're just repeating something that has been accepted in public record in the whole Committee.

DR. WILLIAMSON: This is Dr. Williamson. I would suggest if there's not opposition to it we accept it so that there is a single document, kind of a coherent body, of ACMUI accepted motions.

CHAIRMAN MALMUD: Any further discussion of the motion? If not, all in favor of the motion.

(Chorus of yeses.)

CHAIRMAN MALMUD: Any opposed to the motion?

(No response.)

CHAIRMAN MALMUD: Any abstentions?

(No response.)

CHAIRMAN MALMUD: The motion moves forward unanimously. Thank you. Dr. Williamson, next item.

DR. WILLIAMSON: Okay. We continue. For permanent implants, the Subcommittee did not agree with the above recommendation. So basically there are two recommendations. The first is "the 20 percent absorbed dose threshold is not justifiable for

permanent implants." This was adopted on a 3/0 vote with myself abstaining.

CHAIRMAN MALMUD: That is correct historically.

DR. WILLIAMSON: So I think that is a motion. The rationale is listed here and the reasons detail reasonably well in the report but it's basically felt that due to the limited control the radiation oncologists have on positioning sources accurately, the issues of objectively and reproducibly defining the target volume and so forth, it was felt that a 20 percent threshold is simply too close to the kind of implant-to-implant variability seen in routine clinical practice to be useful as a criterion for distinguishing good implants from bad implants or good QA programs from bad QA programs.

CHAIRMAN MALMUD: Dr. Williamson, are you presenting this as a motion?

DR. WILLIAMSON: Yes.

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

DR. NAG: Yes.

CHAIRMAN MALMUD: It's been moved and seconded by Dr. Nag. Any discussion? All in favor?

(Chorus of yeses.)

CHAIRMAN MALMUD: Any opposed?

(No response.)

CHAIRMAN MALMUD: Any abstentions?

(No response.)

CHAIRMAN MALMUD: It passes unanimously. Thank you. Next, Dr. Williamson.

DR. WILLIAMSON: Okay. The next point is a follow-on to this. "Defining medical events for permanent implants in terms of percent thresholds of absorbed dose delivered to the target volume is not a useful and practical approach." This is basically saying not only is the 20 percent not good but basically this is the wrong approach conceptually to defining a medical event for permanent seed implant.

CHAIRMAN MALMUD: Is there a second to this motion?

DR. NAG: Yes.

CHAIRMAN MALMUD: Dr. Nag.

DR. NAG: Dr. Nag, yes.

CHAIRMAN MALMUD: The motion is open for discussion. Is there any discussion of this motion?

DR. WILLIAMSON: This is an area where I personally had some concerns. So for the record, I would like to note my concerns.

CHAIRMAN MALMUD: Dr. Williamson's concern

is noted, though he has made the motion.

DR. WILLIAMSON: Well, I am Chair of the Subcommittee. It is my duty to make the motion.

CHAIRMAN MALMUD: Yes, we recognize that and appreciate it.

DR. WILLIAMSON: So may I state my concern?

CHAIRMAN MALMUD: Please do.

DR. WILLIAMSON: Okay. The concern is encapsulated in the last paragraph on page three of my report. Basically, in mainstream prostate brachytherapy practice, the authorized user describes treatment intention in units of absorbed dose to the target volume. Through treatment planning, the source strength, number of seeds and seed arrangement are identified to realize this prescription.

So the concerns that I have and this foreshadows future recommendations is that if we omit dose as part of the reporting criterion, then essentially all error pathways related to treatment planning and the conversion of the physician's statement of intention from absorbed dose to number of seeds and total activity will be beyond the scope of regulatory oversight. This seems like a large class of errors to omit from this process and inconsistent

with regulatory approach for other modalities. So that states my concern. I will add the other Subcommittee members recognize this concern and likewise I recognize the appeal and simplicity and unity of the majority approach.

DR. NAG: This is Dr. Nag. I do see Dr. Williamson's point of view. However, historically if you go back in time, the prescription for brachytherapy used to be made in terms of millicuries. Implants even now in some places the prescription for the symmetry for, let's say, cervix cancer and other forms of cancer are made in terms of too many milligram hours. So although in most places, we do prescribe in terms of how much dose, I do not see it being inconsistent to prescribe in terms of millicuries especially for centers that use the approach that for certain volumes you need certain number of millicuries.

CHAIRMAN MALMUD: I hear Dr. Nag.

DR. NAG: Yes.

CHAIRMAN MALMUD: Are you looking for a response?

DR. NAG: No, not really. I just made the statement that although I do see Dr. Williamson's point of view, the point the Subcommittee was making

is not inconsistent with -- medical practice.

CHAIRMAN MALMUD: Thank you. Your concern is noted in the record.

DR. VETTER: This is Dick Vetter.

CHAIRMAN MALMUD: Dr. Vetter.

DR. VETTER: I think there is a corollary with radiopharmaceutical therapy. The nuclear medicine physician wants to give a certain dose to the thyroid for example and he back calculates activity. The prescription actually indicates the activity that would be administered to the patient not the dose to the thyroid.

CHAIRMAN MALMUD: You are of course correct, Dr. Vetter. The prescription however if it varies by 20 percent could fall under this recommendation even though the dose to the thyroid is not really discussed. So that my understanding of this, Dr. Vetter, is that if I were to write a prescription for ten millicuries of I_{131} and if it was plus or minus the ten millicuries irrespective of the dose received by the thyroid, my prescription would valid if it were within 20 percent of the dose that I ordered, meaning the number of millicuries ordered.

DR. VETTER: Yes, I understand that and I think the recommendation of the Subcommittee would

result in the same kind of a scenario for permanent implants. What I'm suggesting is that the two would be consistent with each other.

CHAIRMAN MALMUD: Thank you.

DR. WILLIAMSON: They would be but they would be inconsistent with the current standard of clinical practice. With due respect to Dr. Nag's point, it's certainly true that at one time that maybe a few outlying practices really don't think in terms of absorbed dose for permanent implants. Basically all of the literature in the field is analyzed with respect to absorbed dose to a target volume and all of the current recommendations for how to treat prostate cancer with permanent seed implants are stated in terms of absorbed dose.

So I think it's fine to exempt this activity from regulatory practice, but one should be cognizant of the significance of this. There have been reported significant misadministrations and medical events due to dose calculation errors which would lead to an erroneous estimate of total source strength.

CHAIRMAN MALMUD: We duly note your concern, Dr. Williamson.

MR. LIETO: This is Ralph Lieto. I have

a point of clarification in terms of the report. I don't know if this should be addressed to Tom Essig or the Chair, but will the report itself be an attachment to the minutes of this meeting or incorporated? The reason being that I'm asking this is Dr. Williamson's reservations would be incorporated into the record in total as he specified.

CHAIRMAN MALMUD: It's not a question to me.

MR. LIETO: I don't know who it should be directed to, but I will direct it to the Chair for appropriate redirection.

CHAIRMAN MALMUD: I have to direct it to staff. Tom?

MR. ESSIG: Yes, Dr. Malmud and Mr. Lieto, we can handle it one of two ways. We can, knowing that all that we've said today is part of the transcript. We can certainly include it. It would embedded in there, but I think probably the other way and the way I would prefer to do it is a memorandum recommending with these recommendations that have been voted on today that memorandum on ACMUI letterhead to Dr. Charles Miller.

In fact you could include any minority views as part of the recommendation. Remember in my

opening remarks I said that we valued dissenting or minority views. So an example of that would be that we could include a minority view in the recommendation or as a note right after the individual recommendation.

CHAIRMAN MALMUD: So we do have the opportunity to present this as a matter of information as a minority view.

DR. WILLIAMSON: Yes, we do.

CHAIRMAN MALMUD: Would that be satisfactory, Mr. Lieto and Dr. Williamson?

MR. LIETO: That sounds fine with me.

DR. WILLIAMSON: Yes, no problem.

CHAIRMAN MALMUD: Thank you. May we now move forward on this motion?

DR. ZELAC: Excuse me, Dr. Malmud.

CHAIRMAN MALMUD: Dr. Zelac, yes?

DR. ZELAC: I have a suggestion for consideration by the Advisory Committee.

CHAIRMAN MALMUD: We would love to hear the suggestion.

DR. ZELAC: The suggestion is to look at the motion or the significant recommendation that's being considered now and think about whether it would be improved expanded to include to Dr. Williamson's

concern by adding one word to it as follows. As it reads now, it starts "Defining medical events for permanent implants in terms of percent of thresholds" etc. If we were to consider placing the word "exclusively" after the word "implants" so it would read as follows. "Defining medical events for permanent implants exclusively in terms of percent of thresholds" etc., would that be of any value?

CHAIRMAN MALMUD: It seems to me that it would be. Dr. Williamson, your comment?

DR. WILLIAMSON: I - potentially but in light of the recommendations downstream, I mean I'm not sure it would help. I think that it will perhaps be clear by the time we get to the end of the recommendation I think that this cannot be handled without a revision of the rule. At least, that is my opinion. You will have to see for yourselves. But I think at that time we might entertain additional proposals to consider whether the treatment planning component of the process of planning and delivering such implants should have a role in the revised definition of medical events should that arise in these considerations.

CHAIRMAN MALMUD: Thank you, Dr. Williamson. Dr. Nag, do you have a comment about the

insertion about the adverb "exclusively"?

DR. NAG: No.

CHAIRMAN MALMUD: I'm sorry. I didn't hear you.

DR. NAG: No.

CHAIRMAN MALMUD: No comment. Dr. Vetter.

DR. VETTER: No, I have no comment.

CHAIRMAN MALMUD: All right. So shall we move the motion forward as it is then?

DR. VETTER: I would suggest so.

CHAIRMAN MALMUD: All right. All in favor of the motion?

(Chorus of yeses.)

CHAIRMAN MALMUD: Any opposed?

(No response.)

CHAIRMAN MALMUD: Any abstentions?

DR. WILLIAMSON: I abstain.

CHAIRMAN MALMUD: Dr. Williamson abstains. Okay. Thank you.

DR. WILLIAMSON: Now we come to a more positive suggestion for a replacement strategy for medical events for permanent implants. This is recommendation no. 3. I will read it. Recommendations, here we are, the first bullet. The Subcommittee proposes the following recommendation:

"For permanent implants, the NRC should recommend to licensees that the authorized user specify in the written directive the treatment site in terms of the organ to be implanted (e.g. prostate), the radionuclide and total source strength. A medical event occurs if the source strength actually implanted in the target organ is not within 20 percent of the prescribed total source strength."

CHAIRMAN MALMUD: That is the motion. Is there a second to that motion?

DR. NAG: I would like to modify that last sentence a little bit and that is that if the activity was implanted into the correct target organ, but subsequently migrated to other sites that the portion that migrated would not be within that 30 percent.

DR. WILLIAMSON: Okay. So I think the proposal is to after the occurrence of "20 percent, excluding seed migration,".

DR. NAG: Yes. I think there is already some words similar to that.

DR. WILLIAMSON: That is correct.

CHAIRMAN MALMUD: So the recommendation of Dr. Nag is that your recommendation, Dr. Williamson, have inserted into it after the words "20 percent" a comma and then a --

DR. WILLIAMSON: A phrase.

CHAIRMAN MALMUD: -- prepositional phrase.

DR. WILLIAMSON: Yes.

CHAIRMAN MALMUD: And then a comma and continue on.

DR. WILLIAMSON: That's correct. And the phrase is "excluding seed migration."

CHAIRMAN MALMUD: Very good. Is there a second to that amended motion?

DR. NAG: I second.

DR. WILLIAMSON: Okay. Let me just note a few of the remarks to start off the discussion. This particular recommendation as it stands alone would seem to be implementable without a rule change because of a recent ruling of the Office of General Counsel stating basically that total source strength and absorbed dose are interchangeable in the other brachytherapy category for written directive.

Ralph will correct me if I make any mistakes here about this. There was controversy over the terminology used and I want to be sure that technically the motion we have is correct and precise. The second technical point is in the context of modern brachytherapy practice. Total source strength which is used in the definition of dose for low dose rate

implants in Part 35 is the product of air-kerma strength per see or equivalently apparent activity in mCi and the number of seeds implanted.

This is different from the quantity contained activity which is 25 to 100 percent larger than the apparent activity due to self-absorption infiltration. So I think I'm speaking for the Subcommittee. We really didn't vote on this, but I believe the intent of the Subcommittee was that the concept of total air-kerma strength or equivalently apparent activity was the quantity intended by their recommendation.

DR. NAG: Yes, that is correct. This is Dr. Nag.

CHAIRMAN MALMUD: Dr. Williamson and Dr. Nag agree.

DR. WILLIAMSON: So maybe a question to the staff would be is there any technical or juridical objection to this interpretation?

CHAIRMAN MALMUD: Dr. Williamson is addressing a question to NRC staff regarding this.

DR. ZELAC: Dr. Malmud.

CHAIRMAN MALMUD: Yes, Dr. Zelac.

DR. ZELAC: My opinion, we would always have to get our Office of General Counsel's input, but

my opinion is that is not the most difficulty for this particular regulation grouping. If we were talking however about shipment, transportation, that would be another issue. But in this context, I think using apparent activity should be a satisfactory appropriate.

CHAIRMAN MALMUD: Thank you, Dr. Zelac.

DR. WILLIAMSON: Okay. Well, those are most of my remarks. You can read the other notes those who are interested.

DR. VETTER: This is Dick Vetter. I have a question.

CHAIRMAN MALMUD: Yes, Dr. Vetter.

DR. VETTER: Does the Subcommittee intend to restrict this to organs or does organ include tissues? In other words, today we're talking mostly about prostate implants. Tomorrow we may be talking about some other kind of an implant that might be in a tissue rather than in an organ.

DR. NAG: This is Dr. Nag. The charge to us was stated as for permanent implants especially as applied to prostate. However, I do agree with your concern that we do implant in other areas. For example, we implant tumor beds after reception of the organ because therefore there is no organ that feeds

the tumor bed. But I think if we say off the target area and the target would be the organ, the target would be for example the area and so I think this will still allow you to prescribe as a physician intends to without violating that this is only an organ. I think the area surrounding you can call it some very prosthetic tissue. I mean I think that will be still be allowed.

DR. WILLIAMSON: Let me suggest maybe a potential modification. We could easily modify this to read as follows and that would handle the objection. "For permanent implants, the NRC should recommend to licensees that the AU specify in the written directive the treatment sites..." and then "(for example, the organ to be implanted) the radionuclide and total source strength." That would handle it and reduce the term "organ" rather than being a defining characteristic of treatment site an example.

DR. NAG: One thing, I would say you cannot say "for example, the organ" but you can say "for example the prostate." Because if you say "for example the organ to be implanted, well that is what we are going to implant. So I would say "for example, the prostate."

CHAIRMAN MALMUD: This is Malmud. Would it be acceptable to say "the organ or tissue"? Would that be sufficiently inclusive?

DR. WILLIAMSON: I think so.

DR. NAG: Yeah.

MR. LIETO: This is Ralph. I would definitely say Dr. Malmud's suggestion for amendment.

DR. WILLIAMSON: Okay.

CHAIRMAN MALMUD: Dr. Vetter, do you agree?

DR. VETTER: I missed part of what Ralph said.

CHAIRMAN MALMUD: Ralph agreed with me, but I had suggested inserting "the organ or tissue."

DR. VETTER: Yes, I prefer "the organ or tissue."

CHAIRMAN MALMUD: I'll submit that as an amendment. Are all in favor of the motion as amended?

(Chorus of ayes.)

CHAIRMAN MALMUD: Any abstentions?

(No response.)

CHAIRMAN MALMUD: Any nays?

(No response.)

CHAIRMAN MALMUD: All right. That's unanimous.

MS. SCHWARZ: Dr. Malmud, I have just joined the conference call about ten minutes ago. I apologize for being late.

CHAIRMAN MALMUD: Thank you for joining us. Is that Sally?

MS. SCHWARZ: Yes.

CHAIRMAN MALMUD: Thank you, Sally. Welcome.

MS. McINTOSH: Dr. Malmud. This is Angela McIntosh.

CHAIRMAN MALMUD: Yes, Angela.

MS. McINTOSH: Since there were a couple of amendments to the original recommendation for the record so that we have a clean statement about what is recommended and can't be confused, can you restate in one statement the complete recommendation?

CHAIRMAN MALMUD: Yes. Thank you. Better than my restating it, I will ask Dr. Williamson to restate it.

DR. WILLIAMSON: Okay. The amended motion is as follows. "For permanent implants, the NRC should recommend to licensees that the authorized user specify in the written directive the treatment site, in terms of the organ to be implanted (e.g. prostate), the radionuclide and total source strength. A medical

event occurs if the source strength actually implanted in the treatment site is not within 20 percent, excluding seed migration, of the prescribed total source strength."

CHAIRMAN MALMUD: Thank you, Dr. Williamson. We hope that that is clear for the record. May we move onto the next item?

DR. WILLIAMSON: Yes. The next item is merely advisory. It is the second black bullet near the bottom of page four. It is basically to point out at this point this is a recommendation. Users could continue using absorbed dose. This is simply an item of information that in adjudicatory a medical event, of determining whether an implant is a medical event, when the AU has used absorbed dose to specify written directive would require essentially the licensee and the NRC to agree upon the relevant dosimetric index such as D_{90}, the anatomic target volume, that is the organ and any margin used, and the imaging modality and timing of this imaging procedure used to visualize the target volume.

That if you don't agree on any of these things, if there is disagreement, there could well easily be 20 percent discrepancies just because the individuals involved are not talking about the same

thing. This is not a motion. It is just an information item based upon our December 7th deliberation.

CHAIRMAN MALMUD: Does the information item presented by Dr. Williamson require any further discussion by the members of the Committee?

(No response.)

CHAIRMAN MALMUD: The silence suggests not. Thank you, Jeff.

DR. WILLIAMSON: All right.

DR. NAG: I have one question. Dr. Nag. After that sentence that Jeff read, it says that individual variations may and do deviate by more than 20 percent and these variations do not constitute a medical event. Now if you put that, then if someone is prescribing a dose and has to the prostate and very prostatic organs, what will constitute a medical event then?

DR. WILLIAMSON: A 20 percent variation whatever the authorized user wrote in the written directive. But other dosimetric quantities, other deviations of these, we discussed. You were not there at the teleconference but the staff agreed that under the current medical event definition, 20 percent variations in any of these other quantities would not

constitute a medical event.

CHAIRMAN MALMUD: Does that clarify it for you, Dr. Nag?

DR. NAG: Yes. Just for example if someone writes that the D_{90}, I'm prescribing a D_{90} of 145 grains and the D_{90} turns out not to be within 20 percent of that. That will be a medical event then.

DR. WILLIAMSON: That's correct.

DR. NAG: Well, I mean as along as the authorized user realizes that, I don't know why he would want to open himself to that kind of a problem.

DR. WILLIAMSON: Well, I think that your questions will arise again. As we go through some of the other recommendations, I think it will maybe become clear that it might not be tenable to offer even as a possibility or an alternative to the authorized user to use absorbed dose. So I would suggest maybe we come back to this point if it's relevant after reviewing the other recommendations.

CHAIRMAN MALMUD: Thank you. We'll move on to the next recommendation.

DR. WILLIAMSON: Okay. The next series of recommendations is contained in Issue No. 4. The No. 4 issue can be stated as follows. Is the wrong site medical event criterion, that is 35.3045(a)(3),

workable especially in the case of prostate seed implant? And the Subcommittee thought not. "The Subcommittee unanimously agreed that this criterion is completing impractical clinically for permanent sealed source implants." That is a recommendation that dose-based criterion contained in 35.3045 for wrong-site medical event criterion is completely impractical clinically for permanent sealed source implants.

CHAIRMAN MALMUD: That's a correct summary of the Subcommittee's conclusions.

DR. WILLIAMSON: I believe so.

CHAIRMAN MALMUD: So do we wish to make an motion that we feel that it is an impractical item?

DR. NAG: So moved.

DR. WILLIAMSON: So moved.

CHAIRMAN MALMUD: It's been moved and seconded by Drs. Williamson and Nag. All who would agree?

(Chorus of ayes.)

CHAIRMAN MALMUD: Any opposition?

(No response.)

CHAIRMAN MALMUD: Any abstention?

(No response.)

CHAIRMAN MALMUD: Thank you. Next item, Dr. Williamson.

DR. WILLIAMSON: Okay. The next item is a recommendation to fix this. So the recommendation is "Permanent implants on written directives specifying total source strength implanted in the treatment site should be exempted from the wrong site medical event reporting requirement, 35.3045(a)(3)."

CHAIRMAN MALMUD: Is there a second to Dr. Williamson's motion?

DR. NAG: I think -- I'm not really -- I know we went through some of this, but I don't think we finalize the thing in the Subcommittee. But anyway, let's go on with the discussion. Maybe we come back to it.

CHAIRMAN MALMUD: Okay.

DR. WILLIAMSON: It's on the table. Let me review some of the discussion points that I thought of during the meeting and some that were discussed during the meeting. I think Dr. Nag is right. There are. This is a very complicated issue and there may be some words missing that are necessary. So the main rationale for this proposal is that wrong site medical events would be adequately covered by treatment sites, delivery criteria failures which is paragraph (a)(1) of 3045. Whenever more than 20 percent of the implanted seeds are placed in an organ outside the

target volume, then less than 80 percent of the seeds would remain in the target.

So in kind of why you need to have two separate criteria, the thought was that since we've decided to go to a geometric criterion based on what fraction of the implanted activity is in the target volume, why not incorporate wrong site and over/under dose of the target into a single criterion? I do think it makes since.

A second discussion point is implementing this recommendation would require a rule change. Without changing recommendation three which was the previous recommendation we voted on that medical events should involve 20 percent error in delivering the seeds to the prostate. Without changing three from recommended guidance to a recommended rule revision, eliminating the wrong site criterion might not be practical.

Here we get now to this piece, as we get more deeply into this to come up with a consistent approach, the more radical revision of the whole regulation may be needed. I will note that I had personally, well, sympathetic with this whole general approach of defining wrong site medical event in terms of geometry, basically where the seeds are placed.

I had a technical concern which is at the bottom of page five and top of page six which basically is if an authorized user, or I'll give a hypothetical example, prescribed one hundred seeds to the prostate but accidently implanted one hundred seeds in the rectal wall and the observed this and compensated for this by implanting an additional seeds in the prostate, this individual would comply with the revised 35.3045(a)(1) but by all reasonable estimates, this would still involve a wrong site administration.

My suggestion is to tinker. Well, a suggestion is to basically modify Recommendation 3 to read as follows. "Any implant of the medical event if (a) the total source strength implanted in the patient exceeds the written directive by more than 20 percent OR (b) the total source strength implanted in the target volume deviates from the written directive by more than 20 percent." This would exclude that rather fanciful case. So personally while having sympathy for this approach, I thought technically it needs some work.

CHAIRMAN MALMUD: Any comments?

DR. NAG: Yeah. I think that will still present some difficulty. I mean trying to weed out one very unlikely scenario may introduce a practical

problem for the majority of the practitioners. I think I'm not really happy with it the way it is at the moment, but I want to hear some discussion.

DR. WILLIAMSON: What is the practical problem, Subir?

DR. NAG: I think when we do an implant, let's say other than prostate, we implant a tumor bed and we want to lay as many seeds as we can about one centimeter apart within the tumor bed. We don't really know what exactly is the bond link (PH) and many times technically because of other blood vessels and other tissues you lay as many seeds as you can in the neighborhood of the area you're treating.

It's not a very well-defined organ. How can you say when you are outside your target, when you are inside your target, and I could very easily place more than 20 percent of the seeds in the tumor bed because it is near the tumor bed. So I mean there is a problem if you are trying to implant the prostate and you're implanting the rest and implant it in the wrong site or you are trying to implant the prostate and you implant the penial bulb instead. That's an entirely wrong site, but if you are in the vicinity of that, you may have more than 20 percent of your seeds just outside your target area.

DR. WILLIAMSON: But I would respond that if you look ahead to Recommendation No. 5, that would be a conscious decision on the part of the radiation oncologist to put more seeds than he or she originally anticipated. So a simple follow-up would be simply to revise the written directive because you are able to take advantage of anatomic exposure issues and so on to do a better implant. So you put down 120 seeds within 24 hours and that seems to me to be quite appropriate.

CHAIRMAN MALMUD: This is Dr. Malmud. Jeff, may I ask you a practical question since I'm not a radiotherapist. When ordering seeds from the supplier for the patient, would you normally have that many extra seeds around where someone who was irresponsible and planted 180 rather than 100 seeds?

DR. WILLIAMSON: For prostate, my impression is that skilled physics and radiation oncology practitioners are pretty good about estimating accurately how many seeds they need and depending on the level of experience and the size of the inventory they have, they probably would not order very many more. But I think if haste came about such as Dr. Nag mentioned and the treatment team were clear that the boundaries were not well defined and couldn't

really be appreciated fully until they were in the middle or maybe even near the end of the operative procedure, I think then the physicist would order on the high end based on consultation with radiation oncologists.

DR. NAG: This is Dr. Nag. For prostate, usually you can emate the prostate really well before the procedure until you have an accurate idea of the number of manipuly (PH) you want. But there are many other times when you are implanting tumor bed where the tumor has been receptive and therefore you have no idea how much you are going to place, that you would have higher variation, but that is not a medical event because you are changing or you are making a conscious decision to change at the treatment table.

DR. WILLIAMSON: I think that should be incorporated in any legitimate cluster of definitions of written directive, medical event and rules for allowing revision.

CHAIRMAN MALMUD: Well, my concern, this is Malmud, my concern is that we not become too prescriptive because if we become overly prescriptive, we will create unintended consequences that will limit the ability of physicians to practice medicine in best practice. This also should not exceed our mission

which is the issue of radiation exposure, not the practice of radiation oncology.

DR. NAG: This is Dr. Nag. My feeling on this is that we have said that more or less than 20 percent to the target area will constitute misadministration or medical event. That thing itself should cover ourselves because rather than placing 20 percent to a wrong site, that first definition is enough. It will keep the bad actors away.

DR. WILLIAMSON: Do we have a motion on the table?

DR. NAG: No, not really because we wanted to have this discussion.

DR. WILLIAMSON: The motion on the table is to exempt permanent seed implants from 35.3045(a)(3).

DR. VETTER: This is Dick Vetter. I'm not in my office and can't grab my regulations. Can anyone read that paragraph 35.3045(a)(3)?

DR. WILLIAMSON: I could paraphrase it.

DR. VETTER: All right. Could you please?

DR. ZELAC: Yes, this is Ron Zelac. I could read it. Let me read what's in the preceding materials. This is (a)(3). So (a) is "A licensee shall report any event except for an event that

results from patient intervention in which the administration of byproduct material or radiation from byproduct material results in," now here is three, "a dose to the skin or an organ or tissue other than the treatment site that exceeds by 0.5 sievert (50 rem) to an organ or tissue and 50 percent or more of the dose expected from the administration defined in the written directive exceeding for permanent implants seeds that were implanted in the correct site but migrated outside the treatment site."

DR. WILLIAMSON: I will note for the ACMUI benefit. The reason we didn't like this is that the criterion implies that even if one voxel of normal tissue receives a dose that deviates by 50 centigrade or 50 percent, this could constitute a medical event depending on what you took to be the correct plan. So to us, it seemed like this was a dose, if the dose-based criterion is dubious for specifying the dose to the target volume, a dose-based criterion compared to a geometric criterion is even more dubious for specifying the wrong site.

I think the sense of the Subcommittee is one way or another it should be defined geometrically in terms of where the source is put in the right place or the wrong place and not was the absorbed dose in

excess of 50 percent relative to some other site which is very vague and it's not really been tested by OJC or anyone.

DR. VETTER: But as I understand it in order for to be classified as a medical event, you have to satisfy both criteria, 50 rem to that voxel and 50 percent of the prescription, is that correct, which is based on activity.

DR. ZELAC: The intent is 50 rem or 50 percent of the dose that was expected to be received in the administration by that particular tissue or organ.

DR. VETTER: Okay. So it's totally dose-based.

DR. WILLIAMSON: It is totally dose-based. The proposal, I think, the broad proposal is to, which even I agree with, maybe Dr. Nag no longer does, but at the time the Subcommittee agreed it was reasonable to do away or exempt permanent implants at least from this provision of medical event and make sure that the primary definition of medical event which is activity-based covers wrong site administration. So there would only be essentially one criterion.

DR. NAG: Yes, I think the definition that is there is so vague that I don't think anyone would

be able to enforce it anyway and I think even if we leave it the way it is it doesn't add or take anything away. No matter how you rewrite it, it's very difficult to say what the wrong site is. So even if we leave the way it is, correct me, I don't think the NRC can take any actions at least with the wrong site unless the seed were placed in an absolutely different area of the body.

CHAIRMAN MALMUD: Dr. Nag, this is Dr. Malmud. Do you understand your statement to be stated that you believe that the current regulation as written is sufficiently adequate to cover most situations without restricting unduly the practice of radiation oncology?

DR. NAG: Yes, and that's simply because it's so hard to quantitate what would the dose, that portion of alternated would have been because you can see that. Therefore no one will be able to enforce that in any way.

CHAIRMAN MALMUD: Let me ask a question of you. Has the NRC ever attempted to enforce that in a way which Dr. Williamson was concerned about with respect to the burden borne by even on voxel?

DR. NAG: As far as I know, no, but I think Ron Zelac would be able to say that better than

I would.

CHAIRMAN MALMUD: Dr. Zelac.

DR. ZELAC: Actually even the better source of information if she were on the line would be Dr. Donna Beth Howe. She's been involved in this activity for a goodly long time. However, from conversations that I've had with her, it is my understanding that there has never been such a pointed attempt to enforce this regulation. That there's been the thought of reasonableness that has always entered into any actions associated with events where this might come into play. Keep in mind, of course, that this section 35-3045(a)(3) is intended to apply to all therapeutic modalities and it's in that context that we're now looking at possibly a different approach for permanent implant and permanent implant only.

CHAIRMAN MALMUD: You are correct. Thank you, Dr. Zelac. Since your concern, Dr. Williamson, is a theoretic one which we've not experienced to the best of our knowledge, might you be willing to accept the maintenance of the current wording?

DR. WILLIAMSON: Well, I mean the argument is very strange. The argument is that the regulation is so absurd no one would dare enforce it.

DR. NAG: Exactly.

DR. WILLIAMSON: I would say that's not a very good basis for rule-making in my opinion.

DR. NAG: Yes, but the problem is to make something better is going to be so difficult that I don't think we'll be able to do it in the next 45 minutes.

DR. WILLIAMSON: But it's actually very simple. If we simply extrapolate your very own activity-based criterion one step further, you have a limitation both on the total number of seeds you can place in the patient and the fraction of seeds that must be in the specified treatment site. If one of those criterion is not met within 20 percent, it's a medical event and you have now defined wrong site medical event as any permanent implant in which more than 20 percent of the seeds were unintentionally placed by the physician outside the treatment site.

So now it's no more burden to go back to your post-op example. The first criterion we discussed is no more problem to enforce than this one. So my suggestion would be that it could easily be fixed.

CHAIRMAN MALMUD: This is Malmud. I have a naive question as a non-radiotherapist. I recall that the original discussion related to not only the

placement of the seeds but the migration. Are there instances in which more than 20 percent of the seeds migrate?

DR. NAG: Usually, they are not. The only way I think more than 20 percent may migrate without any harm would be if the seeds were placed in the bladder and the patient automatically either passed it through the urine or we usually go into the bladder and retrieve the seeds. So that probably is the only possible instant. Otherwise, the usual variation to the number of seeds migrating is about two to five percent activity.

CHAIRMAN MALMUD: Then the other part of my question is, I ask this of the radiation oncologists, in the course of good medical practice is it uncommon for more than 20 percent of the seeds to be misplaced.

DR. NAG: It's very uncommon for more than 20 percent to be misplaced when you're talking about the prostate or any defined organ. However if you are having an ill-defined organ where you don't know where that organ is, you could have more than 20 percent outside depending on how you define that volume. That is what I'm afraid of that you can have 20/30 percent outside in the immediate vicinity so that if you tried

to -- more than 20 percent outside the volume and you say the target or the area that you want to implant was in the pancreas and you have more than 20 percent of the seeds just outside the pancreas, someone could mistakenly or if someone wanted to say you wanted to implant the pancreas and now you have 20 percent of the seeds outside the pancreas or just outside the pancreas.

DR. WILLIAMSON: You know my response to that would be that this same objection could be raised against the motion we voted, No. 3, where we said permanent implants that the NRC should recommend to licensees that they specify the written directive in terms of total activity implanted in the treatment site.

The NRC and physicians and everybody, you have to realize what clinical reality is. In certain setting, for example, the post-op case, there is no way to define the target boundary precisely and the only thing you can do is ask the question "Are the seeds reasonably in the correct region of the body" and that's it. You can do no more.

The other dilemma that I think Dr. Nag raises is also false because at the time of the seed implantation, the authorized user always has the right

to revise the written directive upwards if 20 percent more seeds are needed to complete the implant in his or her judgment.

DR. NAG: Exactly, and that is why –

DR. WILLIAMSON: So this is a dilemma.

DR. NAG: Okay. Dr. Nag. That is why I'm saying that, yes, now I can place a few more seeds into the area I want. But the problem is I have more than 20 percent just outside the area and we are making up quantities by putting more seeds inside the area.

DR. WILLIAMSON: Well, then you say that the area is expanded. You have the right to revise the definition of treatment site, too.

DR. NAG: Well, but it's not right to do that anyway. Then I can revise wrongly implanted to rectal and say immediately after I did that, that now I'm going to implant the prostate and the rectal. So if I want to cheat, you cannot prevent me from cheating.

DR. WILLIAMSON: That's correct. We certainly cannot.

DR. NAG: That is why I'm saying rather than making this -- not to make the thing too complicated. So long we are getting to a reasonable

degree, I think we should stop there and not try to make it over complicated.

CHAIRMAN MALMUD: May we get another opinion besides those of Dr. Williamson and Dr. Nag?

DR. VETTER: This is Dick Vetter.

CHAIRMAN MALMUD: Yes.

DR. VETTER: If I may. Since Recommendation 3 specifies the dose or dosage if you will in terms of radionuclide and total source strength, then it makes sense to me if subsequent regulation are also related to radionuclide and total source strength. So I'm trying to understand some of the complexities that Dr. Nag is trying to educate us on. But simply to be consistent, it seems to be that the medical event should be based on source strength rather than dose.

DR. NAG: Yeah, and the medical event we have already discussed and we have already solved that. Now we are talking about the wrong site and what I'm trying to say is that it sometimes can be very complex to say how exactly we define the wrong site. Something that is far removed is very easy to say. Something that is in the near vicinity is very hard to say what exactly is the wrong site.

DR. WILLIAMSON: Agreed. It's very true.

CHAIRMAN MALMUD: Is the wrong site an NRC issue or is it a medical care issue?

DR. SULEIMAN: This is Orhan.

CHAIRMAN MALMUD: Yes.

DR. SULEIMAN: If it's part of the inherent uncertainty with performing the examination, it's a medical issue. If it borders on negligence or somebody did something very wrong, I think it clearly is a regulatory issue.

And let me discuss my perception on the dose. I mean the calculation of absorbed dose is very complex. You have the target volume. You have the activity of the source and a lot of times the activity of the source is synonymously and really incorrectly used as a dose when we're talking about radiation-absorbed dose.

So why not for simplicity focus on what's being administered because that's easy to verify and check, but separate from that, at some point you have to validate the dose that you're calculating. I see these as two separate types of calculations.

I don't know if these recommendations are really addressing that or maybe they should focus on it and the site, are you talking about a proximal site or something that's further away? The further away

you are, the contribution to the dose is going to be less and less significant.

DR. WILLIAMSON: I think the intent of the recommendation was just to basically address wrong site in terms of did you implant the seeds in the right site plus or minus 20 percent or did you put more than 20 percent of the total by mistake into the wrong site, not as a medical intention? So the burden is on the authorized user to specify the medical intention and if necessary, revise it at the time of the procedure.

DR. SULEIMAN: How would this be enforced? How would this be identified?

DR. WILLIAMSON: A typical scenario maybe Ron Zelac or Donna Beth Howe could clarify, but my understanding is in the series of implants mishaps that were identified, prostate implants were found subsequently on, I guess, day after or 30-day later CT imaging. It was incidently discovered that the seeds had been placed essentially in the wrong organ and in some cases, the majority of seeds were placed in the rectal wall or bladder wall. While at the time of the procedure using only ultrasound, the physician thought they were in the prostate. So this was a mistake in terms of interpreting the ultrasound images I guess.

DR. VETTER: This is Dick Vetter. It seems to me that the physician at the completion of the procedure ought to be able to describe what the target volume was and therefore, I'm uncomfortable suggesting that we should exempt these permanent implants from wrong site medical event reporting.

DR. NAG: Now again, I think after I -- I did think about this and from what happened medically. My feeling was that our previous definition of administration of medical implants would catch the wrongdoers and let's not rewrite the definition of the wrong site. Leave the phasing as it is in the -- Part 35 and let's not try to redo that. Sometimes when you redo something, you create more problems than you solve.

DR. VETTER: But is that even applicable since subparagraph (3) is based on dose, not based on source strength?

DR. NAG: I don't know exactly what you're talking about.

DR. VETTER: Well, paragraph 35.3045(a)(3).

DR. NAG: Right.

DR. VETTER: That says it's a medical event if the dose in the extra-target volume tissue is

more than 50 rem or more than 50 percent of, I forgot the exact words, the prescribed dose. Whereas the prescription is not based on dose. It's based on source strength.

DR. NAG: But that is why I'm saying that without even writing anything, you don't even need to say permanent implant at exam because permanent implant are being prescribed differently. I mean this paragraph is something that you really cannot enforce anyway. We didn't want to waste the time trying revise it because it's not applicable anyway. We can put "Not applicable." But to write something that is permanent implant need not or permanent implant statement also at this point, I don't think we really need to.

DR. WILLIAMSON: Well, you know I would guess the reason why this has not been tested by NRC is that everyone's afraid to apply it. If they did, I think there could potentially be thousands and thousands of implants that would agree and if one person decided to test the system and the Office of General Counsel ruled that that was a legitimate interpretation of this, it could cause mayhem. So I honestly think this is a --

The Commissioners have handed us an

opportunity to fix something that's really broken. The activity-based methodology that Dr. Nag has introduced is a potential fix for this. It's very simple and straightforward. It doesn't have all this complexity of dose calculation for permanent implant. I think it's something that should be considered.

MR. LIETO: Jeff and Subir, this is Ralph Lieto. Then basically it sounds like what you are saying in answer to the Item 4 question is we've already addressed it in that first recommendation and really we should just kind of maybe cancel out the reminder of that because what we're trying to do is fix something that obviously is not going to be fixed in a meeting of this length and is going to require a lot more input even if it is fixable.

DR. NAG: Yes, I would say that let's continue with our meeting because we have only half an hour more and there is not going to be any major problem with this the way it is now because you are defining now permanent implant in terms of the termini some much administered activity and you cannot now go back and enforce that you are going to have more than 50 percent of what the dose would have been until I think that it will not apply. So let's --

DR. WILLIAMSON: That is not true, Subir.

The way the rule is written certainly the two parts are independent of one another and they certainly could enforce this. I mean how can you say that.

DR. NAG: How are you going to enforce the thing that you are going to have 50 percent higher dose or -- The other thing is that that would be true even for a removable implant. I mean in a removable implant a certain portion will be getting a pretty high dose. So unless you are really implanting into the wrong area of the body, you really cannot enforce it.

DR. WILLIAMSON: That's why I'm recommending we change it to adhere to that insight that you have just had. Because you notice the last bullet under this point at the top of page six, it basically says this is a problem not only for permanent seed implants but perhaps for all of brachytherapy.

So I think it seems very strange we would, perhaps we can't fix it now and we just leave it. We've already said it's broken. We've agreed with that and we could agree we need maybe to have a more detailed proposal to discuss this at some later time.

CHAIRMAN MALMUD: May I ask another naive question from a non-radiotherapist? It is broken. Is

there any evidence that it has been broken?

DR. NAG: My feeling is that no because I don't think -- You know it's very hard to identify what is a wrong site unless it's totally in a different place of the body. So just leave it slightly vague like it is and then if there's an implant on the left side of the body rather than the right side, it will be applicable right away.

If you are implanting something that's very far away instead you are implanting the liver, you are implanting the pancreas, that's very definite. And if there is some way it is very so vague, you really cannot bring it up. So my feeling is leave this out for the time being.

CHAIRMAN MALMUD: Thank you, Dr. Nag. Let's see. Mr. Lieto, Dr. Vetter, any comments about Dr. Nag's recommendation to be left as it is.

DR. VETTER: Well, I think we're having a little trouble getting past this. So I guess I would agree with Dr. Nag. If we have time, we can come back to it but that we go on for the time being.

CHAIRMAN MALMUD: Thank you.

MS. SCHWARZ: Dr. Malmud. Sally Schwarz.

CHAIRMAN MALMUD: Yes, Sally.

MS. SCHWARZ: I just wanted to mention.

Is it possible since really other than the subcommittee that's dealt with all these issues, we haven't really, I mean it would be nice to have additional time to kind of reread what all has been presented in that maybe we could discuss this again at the April meeting at least this particular point.

CHAIRMAN MALMUD: That's certainly possible.

DR. WILLIAMSON: I think this is very reasonable to simply table this second recommendation under point number four.

CHAIRMAN MALMUD: All right. Let us table -- All in favor of tabling it?

(Chorus of ayes.)

CHAIRMAN MALMUD: Thank you. Let's move on to the next item.

DR. WILLIAMSON: Issue No. 5 is "Does the option of revising the Written Directive as per 35.40(a)(6)(ii) prior to completing the procedure create an opportunity for AUs to avoid reporting technically inferior implants as medical events?" Basically, the answer seems to be yes. There are several cases in which a large fraction of the seeds were implanted in the wrong organ. The AU revised the written directive weeks after performing the procedure

to lower the intended dose arguing that the underdose would be compensated by additional radiotherapy and so forth.

So this has happened and been a concern that I think the ACMUI has been supportive of in the past. The general recommendation the Subcommittee made was that for your consideration "that written directive revisions, intended only to avoid NRC enforcement actions and that do not address legitimate medically-indicated revisions of the treatment plan, are not justified and that either rule changes or changes in enforcement policies should be undertaken to close this loophole." That's recommendation one under part 5.

CHAIRMAN MALMUD: Are there any comments about this recommendation one under part 5 which is on page six of the material?

DR. NAG: The only question someone may have is how can we say that that was made or intended for only to avoid an NRC enforcement. That's the only slight problem I see. I know what we mean, but it's hard to say. It's like going into a legal battle. You do it only to avoid the NRC rules.

DR. WILLIAMSON: Well, we're not making the claim about any specific person. This is a

statement of a problem. It is not a regulation or a rule. So you don't need to have a decidable criterion for applying it.

CHAIRMAN MALMUD: Well, I understand, this is Malmud, Dr. Nag's comment about intent. Perhaps we should simply drop out that part of the statement and leave the rest of the statement in. The SC unanimously agreed that written directive revisions should only at best legitimate medically-indicated reasons.

MS. SCHWARZ: I agree with that revision.

CHAIRMAN MALMUD: Would that be acceptable to you, Jeff?

DR. WILLIAMSON: Yes. Do you want to propose the exact text you have in mind? It's your revision.

CHAIRMAN MALMUD: Okay. "The SC unanimously agreed that written directive revisions should address only legitimate medically-indicated revisions of the treatment plan."

DR. NAG: I think that's plain enough.

DR. WILLIAMSON: Yeah, I think that's fine.

CHAIRMAN MALMUD: If that's a motion, will one of you second it?

MS. SCHWARZ: Second.

CHAIRMAN MALMUD: All in favor?

(Chorus of ayes.)

CHAIRMAN MALMUD: Any nays?

(No response.)

CHAIRMAN MALMUD: All in agreement. Thank you. Next item.

DR. WILLIAMSON: The next proposal is a fix to the problem. "For permanent implants based on written directives specifying total source strength implanted in the treatment site, 35.40(c) and 35.40(b)(6)(iii) should be amended to require completion of the written directive and documentation of any written directive revision within 24 hours of completing the source insertion procedure." That's the recommendation.

35.40(b) and (c) are the definitions of written directive for other brachytherapy. So what this is a proposal to add some verbiage which for permanent implants only would require written directive revisions to be made within 24 hours of the completion of seed insertion.

DR. NAG: Actually, this follows very much the rules for other implants as well. That written directive should be within 24 hours of completion of

the procedure. The only problem in the permanent implant was that there was no indication as when the radiation procedure ever ended and therefore it created a loophole and putting the word "source insertion procedure" does many to close that loophole.

CHAIRMAN MALMUD: This is Malmud. May I make a suggestion that it be within one working day of completion of the source insertion procedure? So that if a department is only open Monday to Friday, it could be done on a Monday for Friday's work.

DR. WILLIAMSON: Seems okay.

MS. SCHWARZ: Yes.

DR. WILLIAMSON: May I make a couple comments about this?

CHAIRMAN MALMUD: Please.

DR. WILLIAMSON: I think in the case where the physician uses source strength and number of seeds, this is reasonable and it's based on the assumption that any medically-legitimate deviation from the original written directive would be known to the authorized user during the implant procedure and would be the result of a conscious decision to alter the implant geometry interoperatively.

Okay. So there is a concern however if this would not be practical for the people who choose

to prescribe use absorbed dose in the written directive because absorbed dose is often not calculated definitively until many weeks after the implant. So therefore a revision of an absorbed dose written directive could not be made within 24 hours of a completion of a permanent prostate seed implant for most practitioners. I want to basically point out that this recommendation is consistent only if the physician writes the written directive in terms of apparent activity.

DR. NAG: Well, that's not necessarily true. I mean first of all you don't want a situation where a practitioner is doing the iso-dose (PH) calculation and then finding that the iso-dose calculation did not meet or did not match with what he had prescribed and then he would change it. So you do not want that time lag anyway.

Secondly, I mean that's the main thing. It's immaterial when they do the dosimetry. You want to know what their intent was at the time of the implant and as they completed the implant. So I think within the 24 hours of completion of the source insertion procedure you would discover their intent.

DR. WILLIAMSON: I think I agree with Dr. Nag's point in general. My only point is that the

recommendation we have voted for previously under Issue No. 3 of our report was that we would recommend to licensees that they specify the written directive in terms of apparent activity, not require. So the problem is that unless we change that recommendation from recommendation to recommend to the users they do this to require the users to do this, there is in inconsistency in the regulations. That's my point.

DR. NAG: This is Dr. Nag. I don't think that's a problem because if I'm prescribing in terms of a dose and let's say I want to give a second amount and while I'm putting my seeds in I find for whatever reason I want to increase or decrease that dose, I can write a revision as I finish my implant saying I wanted to give 10,000 but now I want to give 12,000 or 15,000. But I don't need much more than 24 hours to do that.

DR. WILLIAMSON: What if you don't do imaging of the implant for 30 days and you don't have a treatment plan so you'll never know whether it was 80 gray, 90 gray, 110 gray, 130 gray, 140 gray? You might know but most people --

DR. NAG: Wait. But my intention was to give a second dose. Now if I did not, that's the reason -- I mean if I'm allowed to change my dose

depending on the dosimetry I do later, then I could say that I implant by mistake. I implanted twice or three times the amount and I doubled the dose. I then go back after any implant I planned and I say I initially wanted to give 125 grain. Now I'm giving 250 grain. So I think you are going to defeat the purpose if you allow any revision beyond that 24 hours.

DR. WILLIAMSON: No, you misunderstand. My proposal would be to amend the recommendation in paragraph three to require authorized users to write the written directive in terms of implanted activity. Then there's full consistency in the regulation.

DR. NAG: I don't think you really need to require it. I mean if someone wants to I think it is in the best interest of the authorized user to prescribe it in terms of millicuries but you don't have to force them to use it. I don't think it would be inconsistent. I think a wise authorized user will write in terms of millicuries but if you don't, I mean you could I think if you wanted to have the authorized user avoid having too many unnecessary medical events. You could put it as a suggestion and the reason why you suggest to prescribe in terms of activity rather than those, but I don't think you want to require

them.

DR. WILLIAMSON: I think there is a dilemma here. You know not all revisions of the absorbed dose written directive need be illegitimate. It may be that the authorized user implanted the seeds in a certain way to avoid overdosing the urethra or because of unavoidable anatomic constraints and the dose plan will show a reduced dose and it would be reasonable to put that reduced dose in the chart and maybe contemplate other actions to fix the dose distribution to the prostate or improve it by other treatment modalities or procedures. So I think it leaves a dilemma in place and there's an inconsistency which is not very satisfying which could be easily remedied.

DR. NAG: No, but, this is Dr. Nag, I still feel that if you allow to revise your dose after your permanent implant, after everything has been done, and then you wait a month and then you get dosimetry and then you revise your dose, that is going to open up to anyone who has made a mistake to revise the dosimetry to cover up their mistake. I think that would be major problem if you allow. I'm sorry.

DR. WILLIAMSON: Well, I think that I'm agreeing with you and I'm suggesting it would be fixed

by eliminating it as a possibility.

CHAIRMAN MALMUD: Any other comments besides those of Dr. Nag and Dr. Williamson? So is there a recommendation?

DR. WILLIAMSON: I think there is a recommendation. It's been stated on the table for consideration and a vote.

CHAIRMAN MALMUD: It has been ruled and seconded? Was there a second to that, Dr. Williamson?

DR. NAG: Yes, Dr. Nag seconds.

CHAIRMAN MALMUD: All in favor?

(Chorus of ayes.)

CHAIRMAN MALMUD: Any opposed?

(No response.)

DR. WILLIAMSON: I will abstain.

CHAIRMAN MALMUD: Williamson abstains. All other are in favor. Thank you. Next item.

DR. ZELAC: Excuse me, Dr. Malmud.

CHAIRMAN MALMUD: Yes, Dr. Zelac.

DR. ZELAC: Just for clarification, the recommendation that was just voted on, is it as it appears on page six for permanent implant based on written directives specifying total source strength implanted in the treatment sites?

CHAIRMAN MALMUD: That's my understanding.

DR. WILLIAMSON: I think that's so.

DR. NAG: Yes.

DR. VETTER: That's what I voted for.

DR. ZELAC: Okay. Thank you.

MS. SCHWARZ: Was that changed for the 24 hours to within one working day?

CHAIRMAN MALMUD: Yes, it was.

MS. SCHWARZ: All right.

CHAIRMAN MALMUD: I thought it was. Am I correct, Dr. Williamson?

DR. WILLIAMSON: Let me mention. It appears that this addresses only permanent implants only when the written directive specifies total source strength. So what we are voting on I guess does not address the issue of dose-based written directives. So Dr. Nag's point is still hanging out there and in fact, I can change my vote now and I can vote for this as stated because it's consistent at least.

CHAIRMAN MALMUD: Let the record state that there's unanimity in support of this and that the one changed printing that you see on page six under the third bullet under Item 5 is that instead of saying "within 24 hours" it's "within one working day of completing the source insertion procedure."

DR. WILLIAMSON: That's correct, but it

allows actually the authorized user who writes the written directive in terms of absorbed dose to wait as long as he or she chooses to. So I think that it should be pointed out that is a consequence of this motion.

CHAIRMAN MALMUD: Thank you.

DR. ZELAC: I should point out that the consequence of the motion that Dr. Williamson just described is understood to be an issue by us at NRC as a, if you will, glaring loophole, the kind that Dr. Nag was referring to that the unscrupulous practitioner could take advantage of.

DR. NAG: I think what you could then say you don't need to -- In the previous motion, you don't need to say "based on written directive specifying total source strength" etc. " -- for permanent implant" so and so. You could do it that way.

DR. WILLIAMSON: So there's another new proposal then which strikes out the words "based on written directives specifying total source strength implanted in the treatment site" which could be voted on now, I guess.

CHAIRMAN MALMUD: I have to admit that I've lost track of the statements. May we first reconfirm that bullet no. 3 under Item 5 has been

approved with one change in wording to be "within one working day"?

DR. WILLIAMSON: I believe that's so.

(Chorus of yeses.)

CHAIRMAN MALMUD: All right. It's been approved. Now what is the next motion? Was it in response to Dr. Zelac's concern?

(Chorus of yeses.)

DR. WILLIAMSON: I could make it on behalf of Dr. Nag or he could make it since it's his proposal.

DR. NAG: Yeah. My proposal is that on the previous item that we voted on to prevent the loophole preclusion of striving in terms of dose, we restate that paragraph to say "For permanent implants item 35.40(c) and 35.40(b)(6)(iii) should be amended to require the completion of the written directive and documentation within one working day of completion of the source insertion procedure," basically striking out "written directives specifying total source strength" etc. so that it will apply for both those who are prescribing in terms of dose and to those who are prescribing in terms of activity.

CHAIRMAN MALMUD: Ths is a motion.

DR. VETTER: The consequences of that

would be that a practitioner would not be allowed to do imaging 48 hours later to confirm placement of the sources. He has to do within one working day.

MS. SCHWARZ: Is that a problem?

DR. WILLIAMSON: I think many practitioners would consider it so.

MS. SCHWARZ: Can it then be changed to "within 48 hours"?

DR. NAG: No, but you don't want the practitioner to do the imaging, do a dosimetry and then change his prescription. The prescription or his intent has to be stated before he's implanting and he should be allowed to change it while he's implanting, but not after. I mean if you wait until he's done the dosimetry then he has the ability to change the prescription to show what the dosimetry came out to.

DR. WILLIAMSON: Well, I mean there may be legitimate reasons for doing that actually.

MR. LIETO: This is Ralph. I think basically what we want to do is establish a time line when the treatment has been done as far as the written directive state and I think within one working day is totally acceptable. I think we're going to end up pushing this time period back farther and we're going to be into this is it two days or 30 days. I think we

should leave it right where it's at as already approved.

DR. NAG: The only difference being taking out that phrase "based on written directive specify total source strength."

CHAIRMAN MALMUD: Is that acceptable?

DR. WILLIAMSON: Are you asking for a vote?

CHAIRMAN MALMUD: Yes. This is Malmud. I'm asking for a vote.

DR. VETTER: May I express just one concern?

CHAIRMAN MALMUD: Yes.

DR. VETTER: I don't feel adequately informed about this relative to if you specify the prescription in terms of dose and then while you're doing the procedure, you recognize that something isn't quite as you expected. The motion as stated would require that you do imaging within one working day.

DR. NAG: No, it doesn't require you to do any imaging, what you wanted to -- Imaging is not going to give you the dose. The only way to get the dose is from the imaging to do calculation and do a dosimetry.

DR. VETTER: Right. Yes, I understand that. What I'm saying is if you implant your sources in a pattern other than what you originally intended, then don't you have to re-image or can you with your dose --

DR. NAG: No, basically you need to know your intent, what did you intend to, what dose did you intend to give and basically, that's why from the beginning I have been saying that we should get away from dose and say the medical implant and so on could be defined in terms of the implanted activity.

DR. SULEIMAN: Yes, I agree. The purpose of the imaging in this context is to validate that the number of seeds or whatever is where they were intended.

CHAIRMAN MALMUD: May I ask who just said that?

DR. SULEIMAN: That's Orhan.

CHAIRMAN MALMUD: Thank you, Orhan.

DR. WILLIAMSON: Well, it's not it's only intent. It's other intent is to quantify the absorbed dose you've given the target and the critical anatomy and it's a very important number. The numbers derived from that are very important and they are used in clinical study to rule data from different

institutions.

DR. SULEIMAN: Isn't that a slightly -- I agree but isn't that a slightly different intent? That's where whether it's an unsealed source or a sealed source. You want to valid somehow that the activity is, that the counts that you're seeing with your imager are in fact correlating with the administered radioactivity.

DR. WILLIAMSON: No, I don't think you have the right idea. One doesn't use a radioactivity counting method when a transmission x-ray CT imaging finds where the seeds are, one finds where the prostate and one calculates the 3-D dose distribution.

DR. SULEIMAN: But do you have consensus on your imaging? I just heard ultrasound is used to validate. Are you doing x-ray? Are you doing CT? Are we clear on the imaging modality and how accurate it is in the first place?

DR. WILLIAMSON: Within certain limits, yes. I mean there's a variation among practitioners. Some practitioners do it right away with ultrasound imaging if they are doing intra (Beeping sound) planning. Others would use x-ray, CT day of procedures. Others prefer to wait 30 days and legitimate arguments can be made for all three

methods. Whatever we agree on has to not constrain the practitioner because that's constraining the practice of medicine.

DR. VETTER: This is Dick Vetter. If Dr. Nag who made the motion can live with it, I can certainly support it.

DR. WILLIAMSON: As it's stated, I'm going to vote against it because it's simply inconsistent. I think there are other and more consistent ways of achieving the same goal Dr. Nag wants to achieve which I sympathize with.

MS. SCHWARZ: What other ways, Jeff?

DR. WILLIAMSON: I would suggest go back to issue 3 and revise the written directive to require the written directive to be specified in terms of activity and then the 24 hour rule works and it doesn't punish anybody for doing their imaging at 30 days or one day or anything else. It would be a consistent approach to the problem. Wrong site, wrong dose, written revisions all would be a consistent package. That is I think the virtue of Dr. Nag's original proposal and what we have now is a mishmash of inconsistent dose-based and activity-based prescriptions which I'm uncomfortable with.

DR. VETTER: I agree. I'm actually

uncomfortable with that as well.

DR. SULEIMAN: I'm confused. Why would you validate 30 days after the fact? Why wouldn't you want to do it sooner?

DR. WILLIAMSON: Because many practitioners believe that you can't get an accurate dose plan right after the implant because prostate edema is at its maximum and you need to wait for that to resolve in order to get a better feel for what the average dose is to the prostate.

DR. SULEIMAN: What if there's been a gross migration of the seeds during the implant? What if it hasn't been done properly at all? Or are you saying the ultrasound would solve that initially?

DR. NAG: No, that is the drawback of doing it at 30 days.

DR. SULEIMAN: I mean inherently that just bothers me. I'm not going to lie to you.

DR. WILLIAMSON: The majority of the field I think does it that way. That's my feeling. A lot of people do it at 30 days.

MR. LIETO: Mr. Chair.

CHAIRMAN MALMUD: Yes.

MR. LIETO: This is Ralph. It seems like we have two issues here. One has to do with

validating treatment planning and so forth and the other is to basically establish a QA indicator that what was in the written directive most likely occurred and I think what we've done already has established that.

I'm getting a little confused also because we're making so many changes as we go along. I'm not sure if we're even being consistent with some of the other things that we've done already. And looking at the clock and I know we're going to be hearing somebody pretty soon --

DR. NAG: Two minutes.

MR. LIETO: -- I'm wondering if maybe what we should do is take what we've done so far, distribute it to the committee as a whole and redraft this and try to resolve it, either come up with a final before the April meeting or maybe we might just have to take that long to get all these pieces together. It seems like as we've been digging, the deeper we get the more difficult we're running into other issues like for example what we just had before regarding wrong site. Just a suggestion.

DR. SULEIMAN: I would propose we table this for exactly as Ralph suggested for the April meeting.

CHAIRMAN MALMUD: Dr. Suleiman suggested we table this for the April meeting. Is there a second to that?

DR. VETTER: Second.

CHAIRMAN MALMUD: Any further discussion on tabling this item to the next meeting?

MR. LIETO: This is Ralph again. I would like that we continue to work on this and not wait for our next draft until then because it sounds like there's a lot of other input that might be need from other members for clarity that I think would be very, very valuable, to make this maybe an entire committee project to complete.

DR. NAG: This is Dr. Nag. My strong suggestion would be that we involve at least two or three radiation oncologists who do a lot of permanent seed implants because otherwise the discussion will be between people who are not practically doing the implant. Right now, the only member of the team who is doing this every day is myself.

(Meeting ended due to termination of telephone conference.)

(Whereupon, at 3:00 p.m., the above-entitled matter concluded.)