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NUCLEAR REGULATORY COMMISSION

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ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

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TELECONFERENCE

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THURSDAY, FEBRUARY 15, 2018

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The meeting was convened at 9:06 a.m., Philip Alderson, ACMUI Chairman, presiding.

MEMBERS PRESENT:

PHILIP O. ALDERSON, M.D., Chairman

VASKEN DILSIZIAN, M.D., Nuclear Cardiologist

RONALD D. ENNIS, M.D., Radiation Oncologist

DARLENE F. METTER, M.D., Diagnostic Radiologist

MICHAEL O'HARA, Ph.D., FDA Representative

CHRISTOPHER J. PALESTRO, M.D., Nuclear Medicine Physician

MICHAEL A. SHEETZ, Radiation Safety Officer

JOHN J. SUH, M.D., Radiation Oncologist

LAURA M. WEIL, Patients' Rights Advocate

PAT B. ZANZONICO, Ph.D., Vice Chairman

NON-VOTING MEMBERS PRESENT:

RICHARD GREEN

MEGAN SHOBER

ZOUBIR OUHIB

NRC STAFF PRESENT:

CHRISTIAN EINBERG, Acting Deputy Director, NMSS/MSST

DOUGLAS BOLLOCK, ACMUI Designated Federal Officer

SOPHIE HOLIDAY, ACMUI Alternate Designated Official and ACMUI Coordinator

MARYANN AYOADE, NMSS/MSTR/MSEB

JENNIFER BISHOP, R-III/DNMS

SAID DAIBES, Ph.D., NMSS/MSST/MSEB

JASON DRAPER, R-III

SARA FORSTER, R-III/DNMS

CASSANDRA FRAZIER, R-III/DNMS

MICHELLE HAMMOND, R-IV/DNMS

VINCENT HOLAHAN, Ph.D., NMSS/MSST

PATRICIA JEHLE, OGC

JAN NGUYEN, RI/DNMS

PATTY PELKE, R-III/DNMS

GRETCHEN RIVERA-CAPELLA, NMSS/MSST/MSEB

VERED SHAFFER, RES

NRC STAFF PRESENT (CONT.):

LAURA SHRUM, OGC

DANIEL STROHMEYER, R-III/DNMS

KATHERINE TAPP, Ph.D., NMSS/MSTR/MSEB

FRANK TRAN, R-III/DNMS

LESTER TRIPP, R-I/DNMS

IRENE WU, NMSS/MSST/MSEB

MEMBERS OF THE PUBLIC:

BETTE BLANKENSHIP, American Association of Physicists in Medicine (AAPM)

KELLY CLASSIC, Mayo Clinic

CHARLES CODLEMAN, VA Radioactive Materials Program

THOMAS CONLEY, University of Kansas Medical Center

Whitney Cox, Illinois (IL) Emergency Management Agency

ROBERT DANSEREAU, New York State (NYS) Department of Health

ARIEL DOUCET, Virtua Health

ADAM EKSTEDT, IL Emergency Management Agency

ASFAW FENTA, Virginia (VA) Radioactive Materials Program

MICHAEL FULLER, VA Radioactive Materials Program

MIGUEL DE LA GUARDIA, Cook Children's Health Care System

MEMBERS OF THE PUBLIC (CONT.):

SANDRA GABRIEL, *unaffiliated*

JERRY GEORGE, Baptist Health South Florida

KIMBERLY GILLIAM, VA Radioactive Materials Program

THEODORE GODFREY, Elekta, Inc.

BENNETT GREENSPAN, Society of Nuclear Medicine and Molecular Imaging (SNMMI)

STANLEY HAMPTON, Eli Lilly and Company

STEVE HARRISON, VA Radioactive Materials Program

DESIREE KENNEDY, Elekta, Inc.

RICHARD KENNEY, *unaffiliated*

TIM KLEYN, Indiana University

JANAKI KRISHNAMOOTHY, NYS Department of Health

SUSAN LOHMAN, Elekta, Inc.

LANCHU LU, Ohio State University Medical Center

CAROL MARCUS, University of California at Los Angeles

RICHARD MARTIN, American Association of Physicists in Medicine (AAPM)

BARBARA MATTHEWS, Baptist Memorial Health Care Corporation

CATHERINE PERHAM, Maine Radiation Control Program

RICHARD PEROS, New Jersey Radioactive Materials Program

MEMBERS OF THE PUBLIC (CONT.):

ERIC PERRY, Kentucky Radioactive Materials Section

MICHAEL PETERS, American College of Radiology (ACR)

BRUCE PROCTOR, Elekta.Inc.

BRAD READ, Elekta, Inc.

SLYVIA REVELL, University of Texas Southwestern Medical School

DANIEL SAMSON, NYS Department of Health

BETH SCHILKE, VA Radioactive Materials Program

A. ROBERT SCHLEIPMAN, Partners Healthcare

LOU SHIMABUKU, *unaffiliated*

EUGENIO SILVERSTRINI, Northwell Health

MICHAEL STABIN, Vanderbilt University

CINDY TOMLINSON, American Society of Radiation Oncology (ASTRO)

MICHAEL WELLING, University of Virginia

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

(9:06 a.m.)

CHAIRMAN ALDERSON: Well, good morning, and welcome to today's ACMUI public teleconference. We'll discuss two topics today: nursing mothers' guidelines, the subcommittee report; and the physical presence requirements for the gamma knife, also a subcommittee report.

I will now turn it over to Mr. Doug Bollock from the NRC for some opening remarks.

MR. BOLLOCK: Thank you, Dr. Alderson. Good morning. As the designated federal officer for this meeting, I am pleased to welcome you to the public meeting of the Advisory Committee on Medical Uses of Isotopes.

My name is Doug Bollock. I am the chief of the Medical Safety and Events Assessment Branch, and I have been designated as the federal officer for this Advisory Committee in accordance with 10 CFR Part 7.11.

Present today as the alternate designated federal officer is Sophie Holiday, our ACMUI coordinator.

This announced meeting of the Committee is

being held in accordance with the rules and regulations of the Federal Advisory Committee Act and the Nuclear Regulatory Commission. This meeting is being transcribed by the NRC, and it may also be transcribed or recorded by others. This meeting was announced in the January 23, 2018, edition of the Federal Register on 83 page 3191.

The function of the Committee is to advise the staff on issues and questions that arise on medical uses of byproduct material. The Committee provides counsel to the staff but not determine or direct the actual decisions of the staff or the Commission. The NRC solicits the view of the Committee and values their opinion.

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

At this point, I'd like to perform a roll call of the ACMUI members participating today. Dr. Philip Alderson?

CHAIRMAN ALDERSON: Here.

MR. BOLLOCK: Thank you. Dr. Pat Zanzonico?

VICE CHAIRMAN ZANZONICO: Yes.

MR. BOLLOCK: Thank you. Dr. Vasken Dilsizian?

MEMBER DILSIZIAN: Here.

MR. BOLLOCK: Dr. Ronald Ennis?

MEMBER ENNIS: Here.

MR. BOLLOCK: Thank you. Dr. Darlene Metter?

MEMBER METTER: Here.

MR. BOLLOCK: Thank you. Dr. Michael O'Hara?

MEMBER O'HARA: Here.

MR. BOLLOCK: Thank you. Dr. Christopher Palestro?

MEMBER PALESTRO: Here.

MR. BOLLOCK: Thank you. Mr. Michael Sheetz?

MEMBER SHEETZ: Here.

MR. BOLLOCK: Thank you. Dr. John Suh?

MEMBER SUH: Here.

MR. BOLLOCK: Thank you. And Ms. Laura Weil.

MEMBER WEIL: Here.

MR. BOLLOCK: Thank you. I've confirmed that a quorum is met by the presence of at least six

members.

Also, on the phone do we have Mr. Zoubir Ohib?

MR. OUHIB: Here.

MR. BOLLOCK: Thank you. Mr. Richard Green?

MR. GREEN: Here.

MR. BOLLOCK: Thank you. And Ms. Megan Shober?

MS. SHOBER: Here.

MR. BOLLOCK: All right. Thank you.

Mr. Ouhib has been selected as ACMUI's therapy medical physicist. Mr. Green has been selected as the ACMUI nuclear pharmacist. And Ms. Shober has been selected as the ACMUI Agreement State Representative.

At this time, Mr. Ouhib, Mr. Green, and Ms. Shober are pending security clearance but may participate in the meeting. However, they do not have voting rights at this time.

I now ask NRC staff members who are present to identify themselves. I'll start with individuals in the room here.

MS. HOLIDAY: Sophie Holiday, ACMUI coordinator.

DR. TAPP: Dr. Katie Tapp with the medical team.

MS. WU: Irene Wu with the medical team.

DR. HOLAHAN: Dr. Vincent Holahan, senior advisor.

MR. BOLLOCK: Okay. Now we go to NRC employees on the phone.

MR. BOLLOCK: Maryann, are you with us?

MS. AYOADE: Yes, I am. I had you on mute. Here.

MR. BOLLOCK: Okay. That's Maryann Ayoade, also with the medical team.

MS. AYOADE: That's correct.

MR. BOLLOCK: Anyone else? Any other NRC headquarters employees on the phone?

Okay. Are there any NRC regional employees on the phone?

Okay. Thank you all. Members of the public who notified Ms. Holiday that they would be participating on the teleconference will be captured in the transcripts. Those of you who did not provide prior notification, please contact Ms. Holiday at sophie.holiday@nrc.gov. That's S-O-P-H-I-E dot H-O-L-I-D-A-Y at N-R-C dot G-O-V. Or call her at (301) 415-7865.

We have a bridge line available, and that phone number is (888) 790-6447. The passcode to access the bridge line is 279-0867 followed by the pound key.

This meeting is also using to the GoTo webinar application to view the presentation handouts real time. You can access this by going to www.gotowebinar.com, G-O-T-O-W-E-B-I-N-A-R dot com and searching for the meeting ID 563-775-347.

The purpose of this meeting is to discuss the revised draft report for the ACMUI nursing mother guidelines for the medical administration of radioactive materials, and the revised draft report for the ACMUI physical presence requirements for the Leksell Gamma Knife® Icon™.

Individuals who would like to ask a question or make a comment regarding a specific issue the committee has discussed should request permission to be recognized by the ACMUI chairperson, Dr. Philip Alderson. Dr. Alderson, at his option, may entertain comments or questions from members of the public who are participating with us today.

Comments and questions are usually addressed by the Committee near the end of the presentation after the Committee has fully discussed the topic. We ask that one person speak at a time as

this meeting is also closed caption.

I would also like to add that handouts and an agenda for this meeting are available on the NRC's public website.

At this time, I'd ask that everyone on the call who is not speaking to place their phones on mute. If you do not have the capability to mute your phone, please press star six to utilize the conference line mute and unmute function.

I would ask everyone to exercise care to ensure that background noise is kept at a minimum, as any stray background sounds can be very disruptive on a conference call this large.

At this point, I would like to turn the meeting back over to Dr. Alderson.

CHAIRMAN ALDERSON: Thank you, Mr. Bollock. So I will then start the meeting by turning it to Dr. Darlene Metter, who is the chair of the Nursing Mothers Guidelines Subcommittee. Dr. Metter?

MEMBER METTER: Thank you, Dr. Alderson. And I'd like to first thank the work of my subcommittee members, Dr. Vasken Dilsizian, Dr. Christopher Palestro, and Dr. Pat Zanzonico.

The subcommittee charge was to review the radiation exposure from diagnostic and therapeutic

radiopharmaceuticals, including brachytherapy, to the nursing mother and child.

Now, as a summary of our report in September, we know that many drugs and radiopharmaceuticals administered to the nursing mother can enter her milk, and then, therefore, be ingested by the nursing child. The subcommittee recommendations regarding the radiation exposure to the nursing child follows current existing recommendations for the nursing mother by reputable expert sources such as the NRC, ICRP, Dr. Michael Stabin's paper, and others.

Therefore, our subcommittee recommended -- recommendations mirrored the sources with the use of a maximum dose of 100 millirem to the nursing child. The current literature at times had variable recommendations on the temporary interruption of breastfeeding due to radiopharmaceuticals in the mother's milk, and the subcommittee generally opted to choose the most conservative, which was usually the longest interruption period.

The subcommittee results and recommendations are summarized in a table reviewed at the September 2017 ACMUI meeting. Since that time, there have been comments from Dr. Carol Marcus and Dr.

Michael Stabin, and Dr. Bennett Greenspan and the SNMMI. To review these comments, Dr. Pat Zanzonico will address them and the associated report revisions.

Dr. Zanzonico?

VICE CHAIRMAN ZANZONICO: Thank you, Dr. Metter. So as Dr. Metter just said, we received a number of comments, both from Drs. Marcus and Stabin, and independent from Dr. Greenspan and the Society of Nuclear Medicine and Molecular Imaging. So what I was going to do was step through their respective comments and summarize our responses.

This was an information-dense report, and so there were a number of comments, so please bear with me. The first comment from Drs. Marcus and Stabin was that the draft report failed to describe or at least acknowledge the real and significant benefits of breastfeeding to both the infant and the nursing mother, and they include a statement from the American Academy of Pediatrics to that effect.

And that point is well taken, and in our subsequent revision of the report we think it would be reasonable to include a statement explicitly acknowledging the benefits of breastfeeding to the mother and child, and so we plan to do that in the revised -- the subsequent revision of our report.

The second point was that the so-called specific gamma ray factors cited in Table 2 are incorrect. They indicate by a factor of 1,000. And this was a units transcription error. The values in the table, and as used in our calculations, are in roentgen centimeters squared per microcurie hour.

The mu for micro when it went to hard copy became an 'm' for milli inadvertently. And so the factor of 1,000 error was apparent. We will correct that, of course, in the subsequent revision, but I want to assure everyone that the actual calculations and analyses were based on the actual correct values.

I will just also address the related point of a comment by Dr. Greenspan and the SNMMI. They state in their comments that the specific gamma ray constant, the quantities I'm referring to right now, were in error, and they provided a number of different values with variable units being used.

And of course if we have numerical or other factual errors in the report, those will be corrected and reflected in a revised analysis. However, we asked that Dr. Greenspan and the SNMMI provide a reference for their values. No such reference was provided with their written comments, and so we have no way at this point of verifying their veracity, their accuracy.

Our specific gamma ray constants were taken from a classic textbook in medical physics, Johns and Cunningham, which many of you may be familiar with. So that's the source of our data, but we understand that specific gamma ray constants, like other physical quantities, are periodically updated, and we certainly want to use the most current and most accurate values in our analysis.

And if Dr. Greenspan and the Society can provide a reference, so that we can verify the accuracy of their stated values, we will amend our report accordingly.

The next point from Drs. Marcus and Stabin was they found a number of typos and editorial errors, and we appreciate, of course, their careful reading of the report as we appreciate all their comments and insights, and we will certainly correct these editorial errors in the subsequent revision. Likewise, Dr. Greenspan and the Society noted a number of editorial errors, and we will correct those as well, of course.

One issue that arose, which is always a thorny one, is the system of units to use. We use essentially conventional units because, frankly, that's the system of units most of us, including myself, are most familiar with and most comfortable with. But

we certainly appreciate that we should be transitioning to use of SI units.

And we will confirm with the NRC staff to verify that that's an appropriate thing to do, and we'll amend our report accordingly to use SI rather than conventional units or perhaps SI units primarily with conventional units presented parenthetically. But we will address that point.

A fourth point raised by Drs. Marcus and Stabin was that the dosimetry analysis for radioiodines, specifically with respect to the thyroid, used worst-case factors in terms of maximal uptakes of radioiodine by the thyroid and minimal thyroid gland masses. Both of those conservative assumptions would lead to maximal estimates of dosimetry.

And Drs. Marcus and Stabin recommended that we perform this thyroid dosimetry analysis for all medically used radioiodines, not just I-131. So that would include, of course, I-123, nowadays I-124, perhaps even I-125. And they also suggested that in that analysis we use a range of uptakes, not simply maximal uptake, and a range of age-dependent uptakes and age-dependent thyroid masses. And we can certainly do that.

And, immodestly, I cite my own paper,

Age-Dependent Thyroid-Absorbed Doses for Radiobiologically Significant Radioisotopes of Iodine from Health Physics, 2000. So we can extract dose estimates or -- in the dosimetry analysis from that paper and incorporate the suggested, augmented analysis in the subsequent revision of our report.

Drs. Marcus and Stabin also point out that two significant literature references were not cited in the paper, and certainly we want to be as comprehensive and thorough as possible in incorporating the pertinent scientific literature into our recommendations. And we will certainly review these papers and incorporate them, at least cite them, in our report and, if necessary, make whatever adjustments those dictate.

And they also point out that perhaps an ill-advised phrase was included in the report referencing the available scientific literature on breastfeeding, dosimetry, and so forth; namely, the phrase being the general lack of pertinent data in the literature. And on further reflection, I think we all acknowledge -- and you can verify this by looking at the bibliography -- the references in our report, there actually is already significant literature on the subject. So we will eliminate that phrase as well as

include these additional references.

A further point that was made is that rather than using or modeling he mother and the mother's breast as point sources -- and that is often done, frankly, for simplicity purposes in dose calculations -- we modeled those source regions in terms of the external dose to the nursing baby. We modeled those as line sources based on a paper in the literature, and that yields a more realistic estimate of the external dose to the infant that does a point source model.

Drs. Marcus and Stabin point out, however, that there are so-called humanized gamma ray constants available, certainly at least for I-131. However, we point out -- or we would like to point out that in our calculation we not only model the mother's body and breast as line sources, but we also incorporated the self-absorption of extant gamma rays by those respective source regions, and we also -- well, we modeled those, as I say, as attempting to count the self-absorption.

So we think that our approach, even though we use specific gamma ray constants which implicitly implies -- which implies a point source, we think we've made the necessary adjustments to appropriately quote/unquote "humanize our specific gamma ray constant

values."

I'm just thumbing through my notes. Another point that was made -- and this was a lengthy, very scholarly comment, indicating that basing recommendations with regard to cessation of breastfeeding for mothers who undergo a nuclear medicine procedure, basing that on a 100 millirem limit to the nursing infant is overly conservative, and Drs. Marcus and Stabin recommend a dose limit of five millisieverts instead.

And incorporated into that comment was a strong reputation of the linear non-threshold dose response model for cancer induction by radiation. And I think many of us, myself included, are very empathetic so to speak to that point, and I think many of us have well-founded skepticism about the biological validity of the linear non-threshold model.

But having said that, really, a discussion of that model, as important and interesting as it is certainly, is really beyond the scope of our report. And as Dr. Metter pointed out, we deferred to the prevailing recommendations made by authoritative bodies like the ICRP, NCRP, and so forth.

And we also noted that in their original analysis, in the really seminal and widely cited paper

by Dr. Stabin and Dr. Bryce, that they based their analysis on a one millisievert effective dose quote/unquote limit to the nursing infant.

So based on all of those considerations, and despite our misgivings of the linear non-threshold dose-response models, we decided, as Dr. Metter indicated, to use a one millisievert limit upon which to base our recommendations.

Proceeding now to the comments submitted by Dr. Greenspan and the Society, to address their comment on the possible -- possibly erroneous specific gamma ray constant values, and we will ask them and await the literature citation of the values they cite, and based on our subsequent review of these values in that literature adjust the specific gamma ray constants and our values and our calculations accordingly.

I mentioned that they also had a number of editorial corrections which we will certainly address in a subsequent revision of the paper. And there was a question or a disagreement with our recommendation for discontinuing of breastfeeding following administration of I-123 labeled radiopharmaceuticals, not only sodium iodide but also ortho-iodohippurate and MIGB, metaiodobenzylguanidine, which are all used clinically labeled with I-123.

And I think there may have been a misunderstanding, understandably, given all of the numbers and so forth in the paper, in the report rather, but in Table 2 -- I'm sorry, in Table 5 of the report, in which we include our recommendations on cessation, the penultimate column, the next-to-last column, which use the -- which list the current recommendations of -- that we use here at Memorial Sloan Kettering, indicated a seven-day discontinuation following administration of at least certain I-123 radiopharmaceuticals.

But if you looked at the recommendations for -- from the Committee, which is actually in the very last column of that table, our recommendations are much shorter, no more than 48 hours, and in the case of I-123, iodohippurate, not recommending any interruption of breastfeeding.

So I think we have all -- I think what we -- what the committee or subcommittee has recommended is perfectly consistent with the point that Dr. Greenspan and the Society were making. So, yes, as you see what's on the screen now, in the very last column, the fourth, fifth, and sixth lines refer to cessation of I-123, sodium iodide; metaiodobenzylguanidine, MIGB; and the last of those

three lines, line 6, to ortho-iodohippurate labeled with I-123. So I think our recommendations are consistent with what the Society is recommending.

Dr. Greenspan and the Society are also recommending a more thorough, a more complete dosimetric analysis of radioiodine as a function of age, child age, and thyroid mass. And as I alluded to earlier, we will provide an expanded dosimetric analysis as also recommended by Drs. Marcus and Stabin.

And Dr. Greenspan and the Society also forcefully endorsed the recommendation of Drs. Marcus and Stabin that, number one, a 500 millirem rather than a 100 millirem dose limit or dose benchmark upon which to base recommendations is more appropriate, and that the linear non-threshold model is really not only inappropriate but incorrect.

So I have already addressed that point in my earlier comments. And so that actually completes our point-by-point response to the submitted comments, both by Drs. Marcus and Stabin, and by Dr. Greenspan and the Society. We very much appreciate their careful and thoughtful -- their careful reading of the report and their thoughtful comments. And we have tried to address them as comprehensively as possible. And I think we've done so and will revise the report

accordingly.

So that concludes my comments in terms of our responses to the submitted comments. So, Dr. Metter, I will turn it back to you.

MEMBER METTER: Thank you, Dr. Zanzonico, for a very thorough review and work on the comments from Drs. Marcus, Stabin, Greenspan, and the Society of Nuclear Medicine.

Do I have other comments from our subcommittee members?

Okay. Hearing none --

MEMBER WEIL: Dr. Metter?

MEMBER METTER: Yes.

MEMBER WEIL: This is Laura Weil. I do have a comment, and I'd like to apologize for not submitting it in advance. The subcommittee report recommends the complete cessation of -- states that the cessation of milk production generally occurs about six weeks after the last breastfeeding.

And I encountered a report from the APA, which recommends a longer period of cessation, and I'd like to -- this is from the ATA from 2009 in Thyroid. If I might just briefly read this paragraph and ask for an evaluation of it, basically.

Let's see. Breastfeeding must be stopped

at least six weeks before administration of I-131 therapy, and a delay of three months will more reliably ensure that lactation-associated increase in breast sodium iodide symporter activity has returned to normal.

I wonder if six weeks in our -- in the subcommittee report could be amended to at least six weeks in order to acknowledge the potential for a longer period of time being necessary. I don't know how one would assess how long a period of time between six weeks and three months should be recommended, but certainly for the provision of information to patients, in accordance with the ALARA principles, so that breastfeeding women would have time to allow at least six weeks' cessation of breastfeeding before administration of Iodine-131. Would you comment on that?

MEMBER METTER: Yes. Actually, thanks for bringing that up. There was a comment as far as the minimal timeframe in regards to notifying the nursing mother regarding her I-131 therapy issue with nursing, and we did say it was going to be at six weeks. I have no problem saying at least six weeks prior to the radioiodine administration. Does anybody else on the subcommittee have any comments?

VICE CHAIRMAN ZANZONICO: This is Pat Zanzonico. I have no problem either with that language, meaning specifically 'at least six weeks.' I think we all recognize that both medically and logistically the longer that period of discontinuation of breastfeeding begins prior to therapy, the more problematic it becomes.

And so I think six weeks itself may be somewhat problematic, but I have no problem at all with that language, at least -- at least six weeks for cessation prior to therapy.

MEMBER METTER: Thank you, Dr. Zanzonico. Thank you as well for your comment on that. And any other comments?

Okay. Dr. Alderson, I'll turn it back to you.

CHAIRMAN ALDERSON: Well, thank you. I believe that must conclude this report and discussion. Are there other comments from people who are online?

OPERATOR: And if you have a question or a comment from the phones, you may press star one at this time. Make sure your phone is unmuted and record your name. And to withdraw that request, you may press star two. Once again, press star one for questions or comments from the phones, and I'll stand by for

questions or comments.

One moment. And we do have a question or comment coming from Carol Marcus. Your line is open.

DR. MARCUS: Thank you. Pat, I think we're in complete agreement on everything except the 500 millirem calculations. And I think it would be really helpful to have both the 100 millirem and the 500 millirem, recognizing that for 21 years the limit has been 500 millirem, and then the physician and the lactating mother decide what ALARA provision is appropriate.

Otherwise, what we have is something so conservative that I think a lot of people won't want to use it. I know that Mike and Hazel's paper originally used 100 millirem, but Mike has changed his mind and thinks 500 millirem calculations would be good. And I think having both might be the best way to do it. Then licensees can choose what seems most appropriate, and we'll have at least the calculations with which to make a good choice.

Thank you.

OPERATOR: Does that conclude the question or comment?

DR. MARCUS: Yes, it does.

MEMBER METTER: May I say something on this

regarding -- in our paper, the first part as far as the current guidance, it does allude to a nursing mother who has received, until byproduct material can be released by a licensee, the total effective dose equivalent to any other individual, including her nursing child, is projected to not exceed five millisieverts. But she must give guidance if it's going to exceed one millisievert. So we have that in our paper.

DR. MARCUS: Yes. But you don't have the calculations.

VICE CHAIRMAN ZANZONICO: This is Pat Zanzonico. I personally have no objections to including a -- essentially a dual set of recommendations. I mean, the heart of the report and the key recommendations, of course, are the recommendations for the duration of discontinuing breastfeeding.

And we can certainly add an additional column which gives those periods of time for a 100 millirem dose to the nursing infant and a 500 millirem dose to the nursing infant.

If I understand correctly, the NRC obviously doesn't regulate breastfeeding, and we can provide, as points of information, the recommended

discontinuation periods for 100 and 500 millirem limits, and the patient and their caregivers can then choose as appropriate.

I have no objection, scientific or otherwise, to that approach. I don't know if -- if having dual recommendations in effect is problematic from the NRC's point of view. But from a logistical, scientific point of view, I have no objection to that approach.

MS. HOLIDAY: Dr. Zanzonico and Dr. Metter, NRC does not object to, if you want to amend the subcommittee report to reflect these dual recommendations, that's at your discretion.

MEMBER METTER: Thank you, Sophie. I think if that's okay, we'll go ahead. Any other comments from the subcommittee? Because I think we'll go ahead and make those two recommendations as far as listing on the table as Dr. Zanzonico had reflected.

MEMBER WEIL: This is Laura Weil. Dr. Metter, may I comment on that?

MEMBER METTER: Yes.

MEMBER WEIL: I have no objection to listing both sets of recommendations, but I would like to know that they would be labeled with the agency that recommends both the 100 and the 500 millisieverts

threshold.

MEMBER METTER: Okay.

MEMBER WEIL: So that the chart or the graph itself is labeled to indicate which agencies recommend which threshold.

MEMBER METTER: Okay. I believe most of them are based on the 100 millirem.

MEMBER WEIL: I believe that's true, and I'd like to see that noted in the table.

MEMBER METTER: Oh, I see. Okay. Thank you.

Any other comments?

OPERATOR: And I am currently showing no further questions or comments from the phones. Again, as a reminder, if you have further questions or comments, it is star one. Make sure your phone is unmuted and record your name. And it is star two to withdraw that request. And I'll stand by for any further questions or comments at this time.

MEMBER METTER: Dr. Alderson, I don't think there are other comments or questions at this time.

CHAIRMAN ALDERSON: All right. Thank you very much.

OPERATOR: And we did just have one cue up. If you'd like to wait one moment, I'll get that party's

name.

CHAIRMAN ALDERSON: Certainly.

OPERATOR: One moment. Thank you. Excuse me. Dr. Greenspan, your line is open for your question or comment.

DR. GREENSPAN: Thank you very much. I just had a quick comment as a follow up to Dr. Zanzonico's request for references for gamma ray constants. I'm traveling this week, but I will be glad to provide them next week. I hope that won't be too late. Thank you.

VICE CHAIRMAN ZANZONICO: This is Pat Zanzonico. Yes, Dr. Greenspan, that would be certainly soon enough. The additional analyses I'm committing to are going to take a bit of time, and they certainly won't be concluded by next week, so next week will be soon enough.

DR. GREENSPAN: Thank you very much.

OPERATOR: Thank you. And I'm currently showing no further questions or comments at this time.

CHAIRMAN ALDERSON: Good. Thank you. That means that we will now proceed with the next part of this public conference call. That will be the report from Dr. John Suh's subcommittee on the physical presence requirements for the Gamma Knife Icon. I will

turn the conversation over to Dr. Suh.

MS. HOLIDAY: Dr. Alderson and Dr. Suh, before you launch into the next topic, if I may, can I ask if the Committee will be making a motion to endorse this report with the reflected amendments?

CHAIRMAN ALDERSON: Yes, certainly. That's fine. Let's do that.

MEMBER METTER: Can I make a motion to endorse the amended reports?

PARTICIPANT: Second.

MS. HOLIDAY: And then if you could state for me what the amendments will be, so that we can capture that on the record?

MEMBER METTER: Okay. Dr. Zanzonico?

VICE CHAIRMAN ZANZONICO: Yes. The amendments will include acknowledgment of the benefits of breastfeeding. They will include correction as needed of the specific gamma ray constant values. They will include conversion of the system of units from conventional to SI. There will be an expanded dosimetric analysis of radioiodines as a function of the age and thyroid mass of the child, and also include other medical radionuclides -- radioisotopes of iodine.

We will include at least two additional references as cited by Drs. Marcus and Sabin. And we

will include recommendations or recommended cessation periods of time based on both a 100 and a 500 millirem effective dose to the nursing child.

MS. HOLIDAY: Okay. Thank you, Dr. Zanzonico.

CHAIRMAN ALDERSON: This is Dr. Alderson. I think we should just mention that the transcription errors/typos also will be corrected as recommended.

MS. HOLIDAY: Thank you. Okay. Dr. Alderson, now that there is a motion, can you call for the vote?

CHAIRMAN ALDERSON: All right. All in favor?

(Chorus of ayes.)

CHAIRMAN ALDERSON: Any opposed? (pause) Hearing none, that passes unanimously.

CHAIRMAN ALDERSON: All right. So as I stated a moment ago, I'll repeat now, it is now time for us to consider the report on the physical presence requirements for the Gamma Knife Icon, that subcommittee report. That subcommittee is led by Dr. John Suh. Dr. Suh, you're on.

MEMBER SUH: Okay. Thank you, Dr. Alderson. I want to first thank the subcommittee members, Dr. Ron Ennis and Laura Weil, and also thank Sophie Holiday

for her staff resource support.

So I will -- the charge to the subcommittee was to propose the appropriate physical presence requirements for Leksell Gamma Knife® Icon™ radiosurgery units. And I just want to go through just a little bit about the gamma knife. The gamma knife is a very well-established treatment for patients with various benign and malignant brain tumors, vascular malformations, and functional disorders, including trigeminal neuralgia.

The first gamma knife in the United States was installed at the University of Pittsburgh in 1987, and over the years the gamma knife has evolved and in 2006 the Perfexion™ unit was introduced, which allowed for the authorized users to be inside the treatment unit.

And given the differences between the Perfexion™ versus the models U, B, and C, the Perfexion™ was licensed under 10 CFR 35.1000. And as of the reports, based on information collected, there are 77 Perfexion™ units and 22 Icon™ units in the United States, and worldwide over a million patients have been treated with the gamma knife.

In terms of the current physical presence requirements in 10 CFR part 35, it requires an

authorized user with appropriate training and experience in radiation oncology and an authorized medical physicist to be physically present throughout all treatments involving the unit. And physical presence has undergone some evolution. Initially, it was defined as within hearing distance of normal voice, and as part of a regulatory issue summary it was further defined to be speaking in a normal conversational tone, not a raised voice. And they made a comment that a distance of 20 feet may not be close enough to adequately hear and respond to an emergent situation.

The rationale for changing the physical presence requirements is that the gamma knife unit, as I mentioned, has evolved through the years. It is important that any change we make allow the authorized user to address an emergent situation and also to verify that a correct dose was delivered.

If you look at the past 10 years of the NMED report, there have been 10 reportable events involving the Perfexion™, and only a minority of these events occurred during a treatment.

So from the Perfexion™ in -- there has been an evolution to a newer unit called the Icon™ system. Some of the fundamental differences with the Icon™ system is that it does allow for the option of a

thermoplastic frameless mask rather than a frame. The majority of centers using the Icon™ system still use a frame-based system rather than a mask-based system. It does give the option for those patients who may benefit from some type of fractionated approach.

Number two is it allows the ability to perform integrated stereotactic cone beam CT, which provides stereotactic reference for patient setups.

And number three is it also has a high definition motion management for mask-based treatments, which allows us to confirm that the treatment is being delivered to the target itself.

There was a proposal from Elekta on April 26th about the Gamma Knife® Icon™, and their proposal is that an authorized user and authorized medical physicist be physically present during the initiation of all treatment involving a unit.

Number two is to have an authorized medical physicist present throughout all patient treatments.

And number three is that an authorized user physically be present in the department during patient treatment and immediately be able to come to the treatment room in case of emergency.

Based on the -- looking at the current physical presence requirements, the evolution of the

Icon unit, the recommendations from the subcommittee is that the authorized user and authorized medical physicist be physically present during the initiation of all treatments involving the Icon™, and that the authorized medical physicist be physically present throughout all treatments of the unit itself.

We have made a recommendation that the current physical presence requirements for the authorized user be modified to allow the authorized user to be close enough to the console area to respond quickly to any issues that may arise.

The definition we came up with is that within a two-minute walk of the Icon console area and immediately available to come to the treatment room. So it is very important that with this definition of physical presence, the authorized user cannot be involved in another procedure that would prevent him or her to come immediately to the gamma knife in case of an emergency.

In addition, we felt that it was important that we do not use the definition of a department as "department" can have different meanings to different centers. So one could be stated that it's part of a department, but the department could be physically a long walk away. So we felt that there should be some

time restraint in terms of what constitutes being physical presence in terms of this newer definition.

If there is an interruption of treatment secondary to a medical or mechanical event, the authorized user must return to the Gamma Knife® Icon™ console area to evaluate patient and to review any of the medical -- mechanical issues along with the medical physicist.

And at the conclusion of treatment, the authorized user must be present at the Icon console to discuss any treatment or patient issues with the patient, physicist, and a nurse.

The subcommittee felt that with these modifications, in terms of current physical presence requirements, it would allow more flexibility to the authorized user.

In closing, we felt that it was very important that the committee report did not encroach on the practice of medicine, also allowed for the regulator to inspect the regulated gamma knife center, and also be consistent with regulations governing a physician's supervision.

Any change that occurs to the current physical presence requirements should take into account that the culture of safety quality be supported, given

the superb track record for quality and safety with the gamma knife.

Thank you. That concludes my report, Dr. Alderson.

CHAIRMAN ALDERSON: All right. Thank you. Are there comments?

MEMBER SHEETZ: John, this is Mike Sheetz. I have some comments.

CHAIRMAN ALDERSON: Please.

MEMBER SHEETZ: I think the subcommittee provided an excellent report and overview of the technological advances in gamma knife treatment since the process has become more efficient allowing for more treatments, and multiple targets can be treated in a single session.

And they pointed out, based on the small number of medical events involving modern gamma knife models, it is, therefore, appropriate to evaluate the required physical presence requirements for gamma knife to see if they should be revised.

Based on our experience here at the University of Pittsburgh where we have had every model like the gamma knife, and we were the first to license the U model in 1987, I have some comments with respect to the recommendations of the subcommittee, if I may

proceed with those.

CHAIRMAN ALDERSON: Please.

MEMBER SHEETZ: I agree with the recommendation number one that the AU and AMP need to be physically present at the initiation of all treatments.

With respect to recommendation two, I think the definition of "within a two-minute walk from a gamma knife treatment console" will create ambiguity for the regulatory compliance with licensees, and the recommendation for the appropriately trained staff to be present to respond to patient medical issues is not really enforceable by the NRC.

So I would suggest consideration of this recommendation to be modified to something that actually is in current regulation for HDR right after the initiation of treatment, an authorized medical physicist and either an authorized user or a physician under the supervision of an authorized user who has been trained in the operation of emergency procedures for response of the unit, to be physically present during continuation of all patient treatments involving the unit.

So I'll throw that up for consideration. Again, it would be consistent with the HDR requirements,

and it would eliminate any ambiguity in response times, and it would assure that appropriate personnel are present to respond to any patient medical issues.

I agree with recommendation three that the AU must return to the gamma knife console for the interruption of treatment secondary to medical or mechanical issues.

With respect to recommendation four that requires the AU to be present at the gamma knife treatment console at the conclusion of the treatment to discuss any treatment of patient issues, if the patient treatment has been completed without any issues, I question whether this would be necessary. And if you have eliminated this requirement, it would provide greater relief to the authorized user.

And then the last slide on this, if the subcommittee report -- not specifically saying, but implies some modified physical presence requirements should only be applicable to the Icon™ unit when using the thermoplastic mask for patient treatment and not the stereotactic beam, while the Icon™ utilizes an integrated cone beam CT for stereotactic reference and high-definition motion management systems, these features are only required when using mask-based treatments. They are not required for frame-based

treatments.

In our experience, less than 10 percent of the gamma knife patient cases qualify for mask-based treatments. There have been an extremely low number of medical events with Perfexion™ that have been pointed out involving thousands of patient treatments demonstrating a highly reliable treatment technology.

And so when using the Icon for frame-based treatments, it is identical to the Perfexion™ unit for frame based. So, therefore, I would suggest that the revised physical presence requirements should also be applicable to frame-based treatments on either the Icon or the Perfexion™.

And that concludes my comments.

CHAIRMAN ALDERSON: Thank you. Dr. Suh?

MEMBER SUH: Thank you, Michael, for those very thoughtful comments. So in terms of your second recommendation about whether or not the physical presence requirement of the two-minute walk, this is something that the subcommittee grappled with in terms of what would constitute appropriate physical presence requirements with the Gamma Knife® Icon™, and the number we came up with -- initially, there was some discussion about whether or not being physically present in the department would be adequate, and we all agreed that

that is too -- that is too ambiguous. So we felt that was not a good starting point.

And we grappled at the time -- we needed some type of time standpoint. And I do agree with you that there could be some ambiguity in terms of regulatory compliance. I actually have looked at your comments. I actually thought about it.

And thinking about the HDR model, the current proposal of either an authorized user or a physician under the supervision of an authorized user who has been trained in the operation of emergency response to the unit be physically present during the continuation of all patient treatments involving the unit is a better definition, in my opinion, because it then allows a physician to be present at the console area or within voice distance during the entire treatment.

As you mentioned, the NRC does not regulate the ancillary staff such as nursing support, so that is a consideration that I am certainly open to. I would be curious to see what the other subcommittee members think and also the rest of the committee as well on that particular point.

In terms of point -- so in terms of authorized user returning, I'm glad that you agree with that

comment. I do think it's important for the authorized user to return.

In terms of recommendation number four, I am probably not as strong of an advocate for that. I do believe that the gamma knife does require an authorized user to know what happened during the treatment, and one of my concerns is that if the authorized user does not know that the patient -- because, again, there could be a situation where the treatment is "completed," but things may not have gone as planned. And I think this is an opportunity for the authorized user to deal with the medical physicist to ensure everything has occurred correctly.

Also, from a patient care standpoint, having the authorized user there to let the patient know that everything went well I think is a greater assurance in terms of that the treatment actually did go according to plan rather than having a surrogate physician who has been trained to say, well, treatment went well.

I have found that from a patient standpoint it -- there is a better confidence when the physician is actually there, the one who is actually involved with the actual treatment.

In terms of number five, in terms of whether or not the Icon™ and the Perfexion™ are similar units,

although the fundamental makings of the Icon™ are very similar to the Perfexion™ unit, there is the opportunity to use a cone beam CT device for the frame-based treatments.

What I can share with you is that at our institution about 20 percent of our patients are undergoing frame-based treatments right now, typically up to five treatments -- of treatment. And for our functional cases and for those cases that we -- we have actually started to use the cone beam CT to ensure that the alignment of what we saw on the computer screen aligns with the frame attached to the treatment machine.

So I don't feel that the Perfexion™ and the Icon™ are similar. So I am not in support of modifying physical presence requirements for both Perfexion™ and Icon™. I would propose that we change the physical presence requirements for just the Icon™ unit itself.

MEMBER ENNIS: This is Ron. Just to follow up, being on the subcommittee, my thoughts to Mr. Sheetz's comments. So in terms of the ambiguity of the two-minute walk, well, certainly, there is a little bit of ambiguity with that, although I don't think it will be a lot because it does specify a time which you can measure and walk. And of course people can walk slightly faster or slower, but I don't think it's

tremendously ambiguous.

So I'm comfortable with that. The notion of instead requiring another physician to be there under the supervision, I would be comfortable with that, too. That is more restrictive on our users, I think, than the proposed definition that our subcommittee came up with.

And I think part of our charge was to see whether we could provide safe relief to the authorized user. So I don't know that our constituents, if you will, or the people asking for some relief would feel that we have provided any relief with that. We could maybe hear what those constituents had to say.

But I am comfortable with either, but I do feel like the -- as written in the subcommittee report is kind of aligned with providing some level of relief while still being, you know, conservative in terms of patient safety.

In terms of the other issues, the return at the end I feel is an important component to this as well. In my mind, it's kind of akin at the end of a brachy procedure, kind of -- although we're not requiring formal documentation, that the authorized user documents that everything went as planned, or, if not, what kind of changes.

I do feel like it's really important to close that loop. More subtle things that aren't quite events might not be raised or you might forget about them an hour later when you see each other in the hall. But at that moment, the physicist and/or the nurse or whoever might be there might be able to share some issue about slight patient movement or things like that that could be safety concerns that I think will be lost if there is not that closure at the end.

In terms of the nurse issue, and whether it's appropriate for these guidelines or not, I can kind of certainly see the perspective that it's not something NRC can regulate or does regulate, so it's not appropriate for our subcommittee report. On the other hand, it seems like a good practice advice.

I don't have a good sense of whether good practice advice like this is appropriate or not. I would turn to NRC staff for their comments on that. It feels like a good idea to me, but I do get the argument that it's a little bit more medical than regulatory.

And on the final point of Perfexion™ versus Icon™, frankly, I would defer to Dr. Suh's judgment. He has a lot more experience with these units than I. So I don't have any particular opinion beyond his on that.

I think I covered all the points. But if there is something else, Mr. Sheetz, please remind me.

MEMBER SHEETZ: This is Mike Sheetz. Thank you for your consideration and responding to those -- all of my comments.

So I guess, for clarity, you are recommending these revisions for the Icon™ unit for both frame-based and mask-based treatments. Is that correct?

MEMBER ENNIS: That is correct. Yes.

MEMBER SHEETZ: Okay. The other comment is we -- we do use the cone beam CT with frame based as a replacement for the MRI or co-registration. But otherwise, if we have a frame and an MRI image, we would not repeat the cone beam CT, you know, as a secondary check. And I'm not sure that's standard.

So, again, I guess I still go back to frame-based treatments on Icon™ and Perfexion™ are identical in practice.

MR. OUHIB: Hi. This is Zoubir.

CHAIRMAN ALDERSON: Go ahead.

MR. OUHIB: On item number two, you know, trying to use the HDR regulation type of thing, I think it's a good idea. However, there are institutions that might not be as fortunate to have the luxury of a physician under the direct supervision of an authorized

user.

So perhaps consideration would be to use one or the other; in other words, to keep the two-minute option and perhaps -- or the presence of a physician under the direct supervision of an authorized user.

CHAIRMAN ALDERSON: Are there further comments? Is there anyone that would like to comment on that statement?

MEMBER SUH: This is John Suh. So I can see both points. So in terms of being less restrictive, the two-minute walk from a gamma knife treatment console area is certainly less restrictive. Again, as Ron mentioned, you know, one can walk faster or slower, but, again, I think if someone says two minutes, that's something that the authorized user could work with in terms of what is considered a two-minute walk. Physicians would need to decide what constitutes that as a safety parameter.

You know, in terms of this proposal of either an authorized user or physician under the supervision of authorized user be present, it does -- it's probably a clearer definition, although it is somewhat more restrictive. And for a smaller center that may not have the luxury of having another physician involved, I can see this being a more restrictive definition for

gamma knife.

Not all gamma knife centers have multiple physicians who are: a) trained, and b) have an interest in being involved in gamma knife.

In terms of doing both, I guess I have mixed feelings about whether or not both is a good option. I think we should stick with one option if we are going to go ahead with changing the current physical presence requirements, which was the charge of the subcommittee to begin with.

CHAIRMAN ALDERSON: Further comments? I think we still need to work to clarify this a bit. I'm going to take the prerogative here to indicate what I think is being said, and then I'd like to get, John, your comments and that of the Committee to clarify this.

So I am hearing that regarding the comment of extending this new approach to both the Icon™ and the Perfexion™, I believe that the Committee is saying that it would choose to stay with the Icon™ alone, that there should be -- the physician should be present at the end of the treatment, so that they can talk to the patient.

Am I correct on the Committee's position on those two issues?

MEMBER SUH: This is John Suh speaking again.

Yes, I do believe that the Icon™ and Perfexion™ are different units.

CHAIRMAN ALDERSON: Yes.

MEMBER SUH: And your second point about being present at the conclusion of treatment, like Ron, I feel very strongly that it is important to close the loop when treating patients with high dose/high precision radiation that is offered with the Icon™ Gamma Knife® unit.

CHAIRMAN ALDERSON: Right. Am I correct that Dr. Ennis and Laura Weil agree with those positions?

MEMBER ENNIS: This is Ron. So just to clarify, on the second position of being there at the end, I agree with the position. But to clarify the rationale, for me, it's not just about patient -- you know, good for the patient, the patient will like that, and all that, which I totally agree, but that's really a medical thing.

But I do feel like there could be more subtle or minor safety concerns, issues that might have happened that would not stop the treatment and would not be a misadministration, but might be helpful for the team to know going forward for the next case or the next patient, where things weren't perfect, that

it's really important to have that kind of -- well, they call it a huddle nowadays, right? Doing essentially a mandated huddle from a safety point of view at the end of treatment, which will only really happen efficiently and effectively, in my opinion, if we mandate that everyone gets together at the end.

CHAIRMAN ALDERSON: Yes. Good. Any disagreement with that from Dr. Suh or Ms. Weil?

MEMBER WEIL: No.

MEMBER SUH: No.

CHAIRMAN ALDERSON: Okay. So I think that we have resolved those two issues in terms of the committee's response to the comments. And that leaves us with the comment regarding the two-minute walk versus someone, being the AU or an AU-trained person, being physically present at all times.

I'm going to turn this back to Dr. Suh to try to see if we can navigate our way through that particular concern, which seems to be the significant one remaining in this discussion.

MEMBER SUH: So I have been thinking about this since, you know, Michael sent this to me. As I said, I am -- I like his suggestion, but I do agree that it is more restrictive. And, again, it should be very apparent. You know, a two-minute walk I don't

think should be that ambiguous in terms of responding to an emergency or if there is an issue with a patient.

But my personal feeling, my recommendation, is that the subcommittee report of the altered current physical presence to allow for the authorized user to be within a two-minute walk of the gamma knife console area is appropriate and will allow the authorized user to respond to any immediate medical needs.

CHAIRMAN ALDERSON: Okay. Good. That's definitive. Do Dr. Ennis and Ms. Weil agree?

MEMBER ENNIS: I do.

CHAIRMAN ALDERSON: Laura?

MEMBER WEIL: Yes, I do.

CHAIRMAN ALDERSON: Okay. So that's also clear from the standpoint of the subcommittee. Are there other comments before we open this up to people who might be on the phone lines?

So with the help of the operator, we will now take comments on any of these issues from people who are on the phone?

OPERATOR: Thank you. And, again, as a reminder, if you have a question or a comment from the phone, please press star one at this time. Make sure your phone is unmuted and record your name to introduce your question. And to withdraw that request, you may

press star two. Once again, for questions or comments, press star one and record your name at this time.

And one moment. We'll stand by for questions or comments. One moment, please. And we do have a question or comment from Susan Lohman. Your line is open.

MS. LOHMAN: Thank you. This is Susan Lohman. I am neuroscience applications manager with Elekta. And, first, I'd like to thank the subcommittee for their long and thorough review of this issue, the process that they have gone through.

And at this time, I would like to urge the subcommittee and Committee to move forward with the subcommittee's recommendation as it was proposed and possibly in the future come back to look at the inclusion or continued exclusion of Perfexion™.

And myself, as a representative of Elekta, would be more than willing to provide any subject material necessary to proceed as such.

Thank you.

CHAIRMAN ALDERSON: Do we have other comments?

OPERATOR: Yes, we do have another question or comment. And our next question or comment is from Frank Tran. Your line is open.

MR. TRAN: Yes. This is Frank Tran in Region III, NRC. I have a comment on the rule with the HDR of exactly they -- they didn't require direct supervision from an authorized user or a trained person. It just says under supervision. So I believe the key is not that. So I just want to comment on that.

CHAIRMAN ALDERSON: This is Dr. Alderson. I'd like to ask the commenter to repeat some of what he said, because I don't know how other -- I didn't actually hear all those words very clearly.

MR. TRAN: Okay. So earlier I believe that Mike mentioned about the rule under -- that required authorizer user to be -- or a trained person to be present over the -- under the rule for the HDR. Another person mentioned that there should be direct supervision.

However, under the rule for the HDR, it is not a direct supervision, just a supervision, either direct or not direct. So there's the comment for that.

CHAIRMAN ALDERSON: All right. Did people understand the comment?

PARTICIPANT: Yes.

CHAIRMAN ALDERSON: Okay. Are there further comments?

OPERATOR: I am currently showing no further

questions or comments at this time. And, again, as a reminder, that is star one. Make sure your phone is unmuted and record your name. And it is star two to withdraw that request.

Again, for further questions or comments at this time, please press star one and record your name, and I'll stand by for further questions or comments.

CHAIRMAN ALDERSON: So, Dr. Suh, I'm going to summarize here how I think this conversation has evolved. I think we are -- we have accepted the -- we have listened to all of the comments. We have made comments in return. I believe that we're at the point where we are ready to accept the proposal as it was originally recommended. Is that how you also understand the comments?

MEMBER SUH: Yes, Dr. Alderson.

CHAIRMAN ALDERSON: Okay. Well, in that case, are we in fact ready to -- is the subcommittee and the -- are the ACMUI recommended as -- to accept the report as it was originally proposed? All those in favor?

(Chorus of ayes.)

CHAIRMAN ALDERSON: Any opposed? Thank you. This report is accepted in its original proposed form.

MS. HOLIDAY: Dr. Alderson, if I may, I'm sorry, I didn't catch who made the motion and who seconded the motion.

CHAIRMAN ALDERSON: I believe it was implied that Dr. Suh was making the recommendation, I believe.

MEMBER SUH: Yes. On behalf of the subcommittee, I propose that we accept the current -- sorry, the physical presence requirements of the Leksell Gamma Knife® Icon™ that as submitted on behalf of the subcommittee members.

VICE CHAIRMAN ZANZONICO: Sophie, this is Pat. I'll second it.

MS. HOLIDAY: Thank you.

CHAIRMAN ALDERSON: Good.

MS. HOLIDAY: And then, if I understand, was this a unanimous endorsement, or were there any dissentions or abstentions?

CHAIRMAN ALDERSON: I did ask for that, I believe, and it is a unanimous endorsement.

MS. HOLIDAY: Okay. Thank you.

CHAIRMAN ALDERSON: So is there any other business that we need to conduct this morning?

MS. HOLIDAY: No. I would just like to thank the subcommittee members for putting forth all of the effort for both Dr. Metter's subcommittee and Dr. Suh's

subcommittee, for their thorough reviews and their reports. I would also like to remind the ACMUI members and other participants on the phone that ACMUI will be holding another public teleconference in two weeks on March 1st from 2:00 p.m. to 4:00 p.m. eastern.

The topic of that teleconference will be the subcommittee report for the training and experience requirements under all modalities in 10 CFR part 35 with a focus on 35.300 uses.

The ACMUI will also be holding their spring meeting here at NRC headquarters on March 7th and 8th.

Thank you.

CHAIRMAN ALDERSON: Well, thank for everyone who was on the call today.

Mr. Bollock, anything you would like to say in the end?

MR. BOLLOCK: No, thank you, Dr. Alderson. Appreciate everyone's time.

CHAIRMAN ALDERSON: I believe, Sophie, that we have concluded our business. Thank you all, everyone.

(Whereupon, the discussion of the draft report concluded at 10:19 a.m.)

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February 7, 2018

Advisory Committee on Medical Uses of Isotopes (ACMUI)
U.S. Nuclear Regulatory Commission
11555 Rockville Pike
Rockville, MD 20852

c/o Ms. Sophie Holiday, Sophie.Holiday@nrc.gov

Dear Ms. Holiday and Members of the ACMUI:

We have reviewed the ACMUI subcommittee draft on Nursing Mother Guidelines for the Medical Administration of Radioactive Materials, which is to be discussed at the Feb. 15, 2018 ACMUI meeting. We have a number of comments which we believe should be addressed in the next draft of this document which should make the final document more useful.

1. The draft guidance document assumes theoretical risk to the infant but fails to include information on the benefits of breastfeeding, which are real and significant. According to the American Academy of Pediatrics (AAP):

   "Most health professionals are familiar with the benefits of breastfeeding. The AAP continues to support the unequivocal evidence that breastfeeding protects against a variety of diseases and conditions in the infant such as: bacteremia, diarrhea, respiratory tract infection, necrotizing enterocolitis, otitis media, urinary tract infection, late-onset sepsis in preterm infants, type 1 and type 2 diabetes, lymphoma, leukemia, and Hodgkins' disease, childhood overweight and obesity. There are also maternal health benefits to breastfeeding such as: decreased postpartum bleeding and more rapid uterine involution, decreased menstrual blood loss and increased child spacing (lactational amenorrhea), earlier return to prepregnancy weight, decreased risk of breast and ovarian cancers."

2. We note that the specific gamma ray factors cited in Table 2 are incorrect, by a factor of 1000(!) We hope that this is an error in the table, and that erroneous gamma factors were not used in the calculations given in the document.

3. We note a number of typos that suggest that the document was not carefully reviewed:
    a. In Table 5, the heading "Hazel and Breitz" should be "Stabin and Breitz". "Hazel" is Breitz's first name.
    b. The reference 'Stabin and Breitz' is repeated as references 10, 26, 31, 36, 54, 71, and 73.
    c. The proper spelling of Lu is "lutetium", not "lutecium", but this is misspelled several times in the document.
    d. The word 'radioisotope' is substituted for 'radionuclide' twice. 'Radionuclide' is the general term for a radioactive species; 'isotope' refers to different radioactive species of a given element.
    e. In all cases 'et al' should be 'et al.' (abbreviation mark included).
    f. The name of the computer program is 'OLINDA/EXM'.
    g. Page 8: 'generallyless' is given as one word.
    h. Table 1 – do not capitalize 'rad'.
    i. On page 4 last line and in Table 2 the half-life of F-18 is given as 1.2 hours. The half-life of F-18 is 110 minutes, or 1.83 hours.
    j. It is odd that non-SI units are used preferentially in a 2018 document.

4. For ingestion of radioiodinated pharmaceuticals, the document should contain thyroid dosimetry for all radionuclides of iodine to the infant thyroid as a function of infant uptake and thyroid mass/infant age. Choosing the worst possible case of a newborn with extremely high uptake and a tiny thyroid gland is not useful once the uptake falls from 75%-100% to about 15% and the thyroid mass increases, so a whole range of values needs to be presented. This information is important not only when considering advice to the mother but in evaluating accidents as well, of which there have been a number over the years.

5. We were pleased to see the calculations for external dose to the infant using the mother as a line source instead of a point source. We have two issues, however, with the calculations:
    a. The authors appear to be unaware of important literature on the subject, noting 'the general lack of pertinent data in the literature.' We note, for example:
        i. J. G. Hunt, D. Nosske, D. S. dos Santos. Estimation of the dose to the nursing infant due to direct irradiation from activity present in maternal organs and tissues. Radiation Protection Dosimetry, Volume 113, Issue 3, 28 April 2005, Pages 290–299.
        ii. Mountford PJ and Coakley AJ. Radiopharmaceuticals in breast milk. Proceedings, Fourth International Radiopharmaceutical Dosimetry Symposium, Oak Ridge Associated Universities, Oak Ridge, TN, 1986; 167-180.
    b. In calculating external dose to the infant from the radioactive mother, humanized gamma ray constants should be used or estimated, as the specific gamma ray

constants significantly overestimate infant dose. For example, the humanized gamma ray constant for I-131, with a 364 kev photon, is 1.3, not 2.2 (RADAR Exposure and Dose Calculator, http://www.doseinfo-radar.com/ExposureCalculator.html). For radionuclides with lower photon energy, the humanized gamma ray constants would reflect even more self-absorption by the mother. In the case of a mother with thyroid cancer who has stopped breastfeeding entirely and who has no thyroid of her own (it has been surgically removed), an accurate external dose to the infant after a 5 mCi administration for a metastatic survey and after a 150 mCi administration of a therapy dose should be calculated and appear in this guidance document, so the physician can offer accurate advice about holding the infant and feeding him formula or other milk product.

6. We appreciate that 10CFR35.75 notes a dose limit of 5 mSv (500 mrem) for exposure to members of the public, but requires that guidance be given regarding interruption of breast feeding if the dose to an infant or child may exceed 1 mSv (100 mrem). *We strongly suggest that this second requirement be changed (in the statute) to 5 mSv, and the calculations be redone.* The calculations performed were already conservative, but the application of an additional factor of 5 has no scientific basis. There are no scientifically valid data showing harm to infants at a dose of 500 mrem, and it is therefore unreasonable to reduce the dose far below the legal limit. Every baby conceived and born in Denver, CO has received an extra 500 mrem from background radiation by the age of 15 months, over and above the United States average which is 300 mrem/y. (Background radiation in Denver is about 550 mrem/y). Year after year, the State of Colorado tends to be tied for the third lowest cancer death rate in America, despite the fact that residents receive an extra 250 mrem/y, every year. Some receive even higher doses (Copper City, CO has a background rate of about 890 mrem/y.). By clinging to the Linear No-Threshold (LNT) myth that says any amount of radiation is dangerous and can cause death from cancer, 500 mrem seems five times more dangerous than 100 mrem, but the LNT premise itself has been soundly denounced on various fronts for low dose and dose rates. First, the LNT states that there is no such thing as radiation repair, but we have found over 150 genes that are active in the repair of lesions caused by radiation and metabolism using oxygen, and we know that these repair mechanisms are stimulated by low dose radiation and that they repair more damage than what was caused by the low dose radiation to begin with. We know that one mutation cannot cause a cancer, fatal or otherwise, as assumed by the LNT. If it could, we would see three-year old boys with prostate cancer, five-year old boys and girls with breast cancer, and six-year olds with lung cancer. This does not happen. The LNT states that all doses are additive, and that dose rate is irrelevant. We know that radiation delivered chronically in low doses is much less damaging than the same dose delivered instantaneously. The whole field of radiation oncology is mainly based on the fact that normal tissues can repair if the radiation doses delivered are not too high and repair mechanisms are stimulated, whereas aberrant cancer tissue cannot repair as well as normal tissue. That is why radiation therapy is delivered multiple times over weeks, permitting normal tissue to preferentially repair. If 6000 rad were delivered all at once, you would burn a hole in the patient. It is time to stop using the LNT at low doses as a basis for anything.

Thank you for your attention and consideration. We look forward to reviewing the improved draft.

Sincerely,

Carol S. Marcus, Ph.D., M.D.

Professor of Radiation Oncology, of Molecular and Medical Pharmacology (Nuclear Medicine), and of Radiological Sciences, David Geffen School of Medicine at the University of California at Los Angeles (UCLA) and past two-term member of the ACMUI.

Michael G. Stabin
Chair, RAdiation Dose Assessment Resource (RADAR) Committee of the Society of Nuclear Medicine and Molecular Imaging, and
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SOCIETY OF NUCLEAR MEDICINE AND MOLECULAR IMAGING

February 12, 2018

U.S. Nuclear Regulatory Commission (NRC)
11555 Rockville Pike
Rockville, MD 20852
Washington, DC 20555-0001

Re: Nursing Mother Guidelines for the Medical Administration of Radioactive Materials

Dear members of the ACMUI

The Society of Nuclear Medicine and Molecular Imaging (SNMMI) appreciates the opportunity to comment on the Sub-Committee on Nursing Mother Guidelines for the Medical Administration of Radioactive Materials report drafted by Vasken Dilsizian, MD, Darlene Metter, MD (Chair), Christopher Palestro, MD, and Pat Zanzonico, Ph.D, dated February 1, 2018.

The Society of Nuclear Medicine and Molecular Imaging's more than 17,000 members set the standard for molecular imaging and nuclear medicine practice by creating guidelines, sharing information through journals and meetings, and leading advocacy on key issues that affect molecular imaging and therapy research and practice.

- F-18: 6.952E-4 mrem/hr per uCi at 1 m
- Ga-67: 1.1 x 10-1 mR/hr/mCi at 1 m
- Tc-99m: 1.2 x 10-1 mrem/hr/mCi at 1 m
- I-131: 2.2 R-cm2/mCi-hr

Page 8, line 1, "generallyless" should be two words.

Page 11, #6 (and possibly elsewhere), "lutecium" is correctly spelled "lutetium".

Table 1, "Rad" should be "rad"

Table 2 half life of F-18 is 109 or 110 minutes (depending on the reference, and is therefore 1.82 or 1.83 hours (not 1.2). This is also mentioned incorrectly in the last line of page 4.

Table 5, 3rd column, the reference should be Stabin and Breitz.
References 10, 26, 31, 36, 54, 71 and 73 are all the same reference (Stabin and Breitz).

Additionally, the report offers some debatable recommendations. For example, interrupting breast feeding for 7 days for I-123 400 microcurie capsules. That is significantly longer than 10 half-lives (even though the risk of contamination with other isotopes is no longer present - the previous rationale for interrupting breast feeding). Also, most sources say no interruption of breast feeding is necessary including the NRC regulatory guide 8.39 https://www.nrc.gov/docs/ML0833/ML083300045.pdf (no cessation needed even for doses of 3 mCi) https://www.nrc.gov/materials/miau/miau-reg-initiatives/guide_2002.pdf.

There are certain assumptions of the LNT hypothesis that are lacking in supportive scientific evidence. For one, LNT assumes that there is no DNA repair at low doses. However, the scientific evidence suggests otherwise. There have been over 150 genes identified by radiation biologists that are involved in the repair of DNA radiation damage. There are known to be three types of repair:

1) anti-oxidant prevention
2) enzymatic repair of DNA damage
3) removal of DNA alterations by apoptosis.

Another assumption of the LNT that needs to be addressed is that the dose rate does not matter. However, that supposition is also not supported by scientific evidence. In fact, the entire field of Radiation Oncology is based on repair of radiation damage, and particularly that the repair mechanisms of normal tissue are more efficient than those of cancerous tissue.

SNMMI appreciates the opportunity to comment on this report. As always, SNMMI is ready to discuss any of its comments or meet with NRC on the above issues. In this regard, please contact Caitlin Kubler, Senior Manager, Regulatory Affairs, by email at ckubler@snmmi.org or by phone at 703-326-1190.

Sincerely,

Bennett S. Greenspan, MD, M.S.

Bennett S. Greenspan, MD, FACNM, FACR
President, SNMMI