UNITED STATES OF AMERICA

NUCLEAR REGULATORY COMMISSION

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MEETING WITH THE ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

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THURSDAY,

MARCH 17, 2016

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ROCKVILLE, MARYLAND

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The Commission met in the Commissioners' Hearing Room at the Nuclear Regulatory Commission, One White Flint North, 11555 Rockville Pike, at 9:30 a.m., Stephen G. Burns, Chairman, presiding.

COMMISSION MEMBERS:

STEPHEN G. BURNS, Chairman

KRISTINE L. SVINICKI, Commissioner

WILLIAM C. OSTENDORFF, Commissioner

JEFF BARAN, Commissioner

ALSO PRESENT:

ANNETTE L. VIETTI-COOK, Secretary of the Commission

MARGARET M. DOANE, General Counsel

ACMUI PANEL:

PHILIP O. ALDERSON, M.D., ACMUI Chair

STEVEN R. MATTMULLER, ACMUI Nuclear Pharmacist

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

LAURA M. WEIL, ACMUI Patients' Rights Advocate

PAT B. ZANZONICO, Ph.D., ACMUI Vice Chair

P R O C E E D I N G S

9:30 a.m.

CHAIRMAN BURNS: Good morning, everyone. I want to welcome you to our meeting today with our Advisory Committee on the Medical Uses of Isotopes. I welcome the members here today.

The Commission will be holding a meeting in order to hear views of the Committee members to provide on significant issues that have come before them.

Before we being, on behalf of the Commission, I would like to take this opportunity to congratulate Dr. Philip Alderson for being appointed as Chairman of the Advisory Committee and Dr. Pat Zanzonico for being appointed as Vice Chairman of the Committee in October of 2015. Dr. Alderson has served on the Committee since 2014, and Dr. Zanzonico has been on the Committee since 2010. We are very fortunate to have you serve in these roles, and we appreciate it.

Today we will be briefed by several members of the Committee on various topics, including an overview of activities of the Advisory Committee. We will hear, also, comments on the NRC's Patient Release Project. Ms. Weil, the Patients' Rights Advocate, will provide comments on that project.

Other members who are here, Dr. Palestro, a nuclear medicine physician on the Committee, will discuss the Committee's comments on training and experience requirements for authorized users of alpha and beta emitters. And Mr. Steven Mattmuller, a nuclear pharmacist member on the Committee, will discuss

decommissioning funding plan requirements for the medical use of germanium-68/gallium-68 generators. I think Chairman Alderson is also going to provide some comments on enhancing communications.

After the presentations, we will have a question-and-answer period with the Commission. Before I begin, any of my colleagues have any comments?

(No response.)

All right. Then, I will turn it over to you, Dr. Alderson.

DR. ALDERSON: Thank you.

Good morning, and thank you, Chairman Burns and the Commissioners, for meeting with us today.

My name is Dr. Phil Alderson, and I am the ACMUI Chairman. Today I will give you an overview of the ACMUI's purpose, of activities that the Committee has performed since the last Commission meeting, as well as continuing current activities.

The next slide, please.

The ACMUI exists to advise the NRC staff, and, thus, you, the Commission, on the policy for medical uses of radionuclides and, also, to provide technical assistance and to serve as consultants.

There are 13 physicians -- next slide, please -- on the ACMUI, six physicians, two physicists, one radiation safety officer, one patients' rights advocate, and two governmental representatives.

Next slide, please.

Some topics addressed by the ACMUI in the last year include refining some aspects of 10 CFR Part 35 rulemaking, including NUREG-1556, Volume 9; revising the NRC's Abnormal Occurrence

Criteria as the criteria relate to medical events; medical events themselves for all medical applications, with particular attention -- next slide, please -- to those involving yttrium-90-labeled microspheres; the training and experience requirements for 10 CFR 35.390 AUs, Authorized Users, of alpha and beta emitters.

Next slide, please.

Revisions to the NRC's Radioactive Seed Localization Licensing Guidance and the decommissioning funding plan requirements for the medical uses of germanium-68/gallium-68 generators.

Next slide, please.

A clarification of the term "patient intervention" and review and consideration of three petitions for rulemaking related to the LNT Model and standards for protection against radiation.

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The current ACMUI topics include continuing discussions that involve patient release, review of medical events, medical event reporting for all modalities, and training and experience requirements for Authorized Users of alpha and beta emitters.

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Additional continuing topics include Radioactive Seed Localization Licensing Guidance; addressing the decommissioning funding plan requirements for the medical use of germanium-68/gallium-68 generators; the Leksell Gamma Knife Icon Licensing Guidance.

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And ways to enhance communications between the NRC staff, the ACMUI, and the medical community.

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The ACMUI currently has a number of issues under discussion. As new issues arise, including emerging technologies, we will address and provide advice on aspects relevant to the safe handling of radioactive sources.

At this time, I would like to turn to Vice Chair Pat Zanzonico to begin more focused discussions.

DR. ZANZONICO: Thank you, Dr. Alderson, and thank you, Commission, for the opportunity to present.

Could I have the first slide, please?

I would like to emphasize that these comments do not necessarily reflect a unanimous, or even necessarily majority, opinion of the ACMUI on the NRC's ongoing Patient Release Project. Further, the ACMUI has not yet had the opportunity to review the work to date by the NRC staff on that project. So, this is some tentative or to-date comments on this project.

The next slide, please.

I first wanted to take the opportunity, as long as we had it, to re-endorse the use of radiation dose- versus activity-based release criteria for radionuclide therapy patients. It is important to emphasize this is strictly within the context of radionuclide therapy and not necessarily other contexts.

Needless to say, the health benefits of radionuclides in general and radionuclide therapy, in particular, are widely recognized

and established. Although there is some difference of opinion, in my opinion, certainly, the doses to the public which we are discussing are really of the order of background doses. And so, given these considerations, I think that there is unanimity of opinion that excessive regulatory control on radionuclide therapy and related issues should be avoided.

Next slide, please.

Further, and by way of a prologue, radiation dose is certainly a more meaningful and direct metric of radiation risk than is activity. It has been demonstrated in a number of ways the amount of radioactivity or the activity in a radionuclide therapy patient really is not a reliable predictor or indicator of radiation dose to other individuals from a radionuclide-therapy-treated patient.

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So, again, we would like to take this opportunity to re-endorse the current regulation which promulgates a dose-based rather than activity-based release criterion for radionuclide therapy patients. The ACMUI remains convinced that that is certainly the more appropriate, the more scientifically-sound approach to formulating release criteria.

Next slide, please.

So, again, the NRC, through its Patient Release Project, is developing at patient-directed website and related documentation, specifically, a brochure providing information on radionuclide therapy, and specifically, iodine-131 sodium iodide treatment for thyroid diseases related to patient release and other

patient safety issues.

Now this is an ongoing project. As I said initially, the ACMUI has not yet had the opportunity to see the work product to date. So, this is not specifically a commentary on that work to date, but more on the general concept, the general principle of an NRC website and related materials.

Next slide, please.

What I would like to emphasize is that there is wide variability in the quantity and quality of radiation safety and related information conveyed from physicians, treating physicians, to their patients. There is no disputing that. As I said, there is wide variability in quality and quantity.

Now some of this variability is legitimate in the sense that it reflects differences among patients in terms of their treatments and in terms of their living in other circumstances. But certainly there is a component that is just simply due to a lack of a systematic dissemination of such information from physicians to patients.

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So, given that, there certainly is a pressing need for formulation and dissemination of systematic data that is clear, consistent, and scientifically-based related to radiation safety information that is conveyed to patients. At least myself and a number of other members of the ACMUI, though not all of them, feel that there is already adequate such information in the peer-reviewed medical literature and that the issue is not one of regulation, but, rather, of professional education.

Next slide, please.

Just as one example of this -- and in terms of full disclosure, I was a coauthor of this NCRP Report -- but NCRP Report No. 155, entitled "Management of Radionuclide Therapy Patients," dealt in-depth with issues of patient release, not only in the context of iodine-131 sodium iodide therapy, but for many other isotopes and many other therapeutic agents, dealt with the issues of patient release and related radiation safety issues, including post-release precautions, including disposal of household waste, which I should take the opportunity to say we certainly endorse that such waste should be handled in the general waste stream and certainly not sequestered or returned to the hospital or any such thing as that.

That aside, among the features of this report is an Excel file which, based on some very simple and limited number of measured patient values and parameters, will yield a patient's specific time of release and duration of variation post-release precautions. This Excel file, then, populates a two-page patient-specific instruction sheet which can be given to the patient. We have distributed this Excel file and related documentation to already over 50 centers.

For any of you who are familiar with the NCRP reporting process, they are very thoroughly and critically vetted by the scientific community. So, this is just one example of available resources to professionals that already deal, we feel, rigorously with this entire issue.

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And so, the inadequacy and inconsistency in radiation

safety information, to the extent it exists, is really a matter of professional education that at least some of us on the ACMUI feel is most appropriately and most effectively handled not through a regulatory agency, but, rather, through physician education in terms of, for example, professional societies' practice guidelines.

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So, given that at least some of us feel that a patient-directed website and brochure, however well-intended and however rigorously vetted, is really inappropriate because it effectively interposes a regulator, in this instance the NRC, between the patient and his or her physician. To some extent, it could actually exacerbate confusion and anxiety among patients and to some extent among the general public in that it inevitably fails to account for patient-specific differences in living circumstances and other issues.

Next slide, please.

So, that concludes my comments. I would now like to introduce the ACMUI Patient Advocate, Ms. Laura Weil.

MS. WEIL: Thank you, Dr. Zanzonico, and thank you for the opportunity to present some perspective on the Patient Release Project from the point of view of a patient advocate.

I would like to make one comment on Dr. Zanzonico's presentation before I go into my own, which is his assertion that iodine-131 really won't result in public exposures above background. But I would like to make the point that, unless good patient release instructions are provided and understood by the patient, indeed, iodine-131 patients may expose the public to greater-than-background

levels of radiation.

The Patient Release Project has some significant benefits as well as some potential shortcomings in its concepts. One of the major benefits is that it creates an opportunity for professional organizations, individual clinicians, and patients to review procedures for release of iodine-131 patients in the context of best clinical practices.

It also creates a potential for reconciliation of discrepancies in the instructions patients receive for radiation protections for family and the public in the post-treatment period, and it creates opportunity for framing for patients how they can access additional information, advocate for themselves, and generally be knowledgeable about their care and how to protect the public. The website that is proposed is not specifically patient-directed, but, rather, directed to the entire community of clinicians and organizations and patients who are involved in iodine-131 therapy.

The potential shortcomings include that the project may not address issues of access to information and instruction for patients with limited literacy or limited English proficiency. Given the passive collection aspect of the project which relies on the medical community and the public to submit material, the receipt of patient education information and materials in video or translated formats may be less than what is needed. In addition, passive data material collection may not elicit information from small sites that are not connected to academic sites or the professional organizational networks.

Iodine-131 therapy is delivered in a broad array of venues. Guidance that is appropriate for one kind of medical setting may not be completely relevant for another kind of setting. The logistics of delivering care in the community differ from the delivery in large tertiary care facilities. Resources vary.

For example, not all patients may have access to a nuclear medicine physician. So, patient education materials that recommend making an appointment with a nuclear medicine physician may not be appropriate for all patients. Expectations created on the web portal for care in larger medical centers may not be realized in the non-hospital or community setting.

The assertion that regulating the provision of information to patients on how to protect the public from radiation exposure after iodine-131 therapy is interfering in the practice of medicine is misguided, in my opinion. Regulating how patients are informed about protecting members of the public from radiation exposure is a matter of public health, well within the purview of regulation.

The purpose of the Patient Release Project is to assist in the development of guidance for licensees and information for patients, but guidance without the teeth of regulation is intrinsically vague and disjointed and provides poor protection for the public.

Thank you.

I will turn the microphone over to Dr. Palestro.

DR. PALESTRO: Thank you.

May I have the first slide, please?

My name is Chris Palestro, and I am the nuclear medicine physician member of the ACMUI. I appreciate the opportunity to provide some comments on training and experience requirements for the Authorized Users of alpha and beta emitters.

Next slide, please.

By way of some background, radioimmunotherapy of lymphoma with beta emitters was approved about 14 years ago. Two agents were approved at that time, yttrium-90 ibritumomab tiuxetan, which is known as Zevalin, and iodine-131 tositumomab; the trade name is Bexxar.

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The use of both of these agents peaked shortly after their introduction and has steadily declined since then. Bexxar, in fact, was withdrawn in 2014 because of a lack of use, when fewer than 75 patients were treated.

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This slide simply illustrates a decreasing use of Zevalin over the course of the past nine or ten years.

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Why has radioimmunotherapy use declined despite favorable clinical results? Is it, in fact, the direct effect of the change in Authorized User training and experience requirements that went into effect in 2006? Well, the ACMUI formed a subcommittee to look into this matter.

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Our first charge was to determine if the current

requirement of 700 hours for training and experience for Authorized Users of alpha and beta emitters places hardship on the patient community and to make recommendations for ACMUI action.

Next slide.

Our second charge was to establish a recommendation for the total number of hours of training and experience for Authorized Users of such emitters that appropriately balances safety with reasonable patient access.

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Well, we sought to examine some of the factors that could possibly account for decreased radioimmunotherapy use. One factor is a lack of knowledge. Trainees, residents, fellows in hemotology/oncology are not exposed to radioimmunotherapy during their training. It stands to reason that, if they are not exposed to it during training, they are not going to be familiar with it when they enter practice and they are going to be less likely to order these therapies, if they are going to order them at all. However, a lack of knowledge about these agents really isn't a regulatory issue; it is an educational issue.

What about competition from other drugs? These agents, as I just mentioned, were approved more than a decade ago, and research into treatment of lymphoma has continued since that time. There have, in fact, been new agents that have become available. Some of these agents are as efficacious, and in some cases potentially more efficacious, than radioimmunotherapy. It stands to reason that these alternatives in certain circumstances will be used rather than

radioimmunotherapy. That, too, can explain some of the decrease in use of these agents.

It is important to point out that this is not unique to radiotherapy, to radiation or radioimmunotherapy, that this, in fact, occurs with all sorts of therapeutic and even diagnostic procedures. As newer and more efficacious or equally efficacious, but less complicated procedures become available, they are going to be used.

Next slide, please. I'm sorry, can we go back one slide?

What about a shortage of Authorized Users? In his letter of February 2016 to the ACMUI, Dr. Steven Mace, who is an Authorized User and an oncologist in Florida, stated that he is unaware of a single oncologist who has become an Authorized User since the change in the training and experience requirements went into effect.

Unfortunately, it is difficult to judge the significance of that statement because we have no knowledge of how many Authorized Users there were prior to the change in rules and regulations. In order to determine the effect of any change, be it an increase or decrease in rules for training and experience, or for anything else for that matter, we really need to have aggregate data over time, data which, unfortunately, are not available.

Next slide.

Further undermining the position that a lack of Authorized Users is responsible for a decrease in the use of these agents is the fact that, even at large institutions where there is an abundance of Authorized Users, these agents are used very

infrequently, as you can see from this slide. These are just some selected but, nevertheless, quite large institutions where these agents are used very infrequently.

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So, the Subcommittee concluded that the explanation for the decreased use of radioimmunotherapy is likely multifactorial, that the shortage of Authorized Users is certainly not the only, nor is it likely to be the primary explanation for this decreased use. Having said that, however, regardless of that, why not reduce the training and experience requirements?

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The argument in favor of that is that there is an excellent safety record for radioimmunotherapy and that there is precedent for an alternative reduced training and experience requirement with the 80 hours for training and experience for I-131.

But let's look, first, at the excellent safety record for radioimmunotherapy. It is important to recognize that in the vast majority of instances these radiopharmaceuticals have been administered by or in conjunction with Authorized Users who have undergone the more extensive, rigorous training and experience. By that, I mean nuclear physicians, radiation oncologists, and nuclear radiologists. Whether or not it is possible to extrapolate that safety record to individuals with considerably less training and experience really is a matter of conjecture.

With respect to iodine-131 therapy, it is important to note, also, that endocrinology has a long and intimate history of

involvement with radioactive iodine by virtue of its use for diagnosis and therapy of a variety of thyroid diseases. The field of nuclear medicine, in fact, to a very great extent originated in or was really born out of endocrinology and, again, radioactive iodine and thyroid disease.

What about the consequences of misadministrations? Or I should say it is getting back to safety in terms of radioimmunotherapy versus I-131. It has been stated that I-131, in fact, in some circumstances it may be more hazardous and more complicated than radioimmunotherapy.

Well, there are a couple of differences that need to be pointed out. No. 1, iodine-131 is given orally, and in the vast majority of cases it is given in a capsular form. So that, if it drops out of a patient's mouth, that capsule, or it drops out of the vial onto the table or onto the floor, the cleanup is relatively neat and efficacious and safe.

On the other hand, if we are talking about radioimmunotherapy, it is a liquid. It is clear. It is colorless. It is odorless. If that vial shatters, if due a mispositioning or an incorrect arrangement for the injection, it winds up on the floor or on personnel. It has to be cleaned up and it is more difficult to clean up a liquid than a solid. Furthermore, it is more difficult to determine activity when we are dealing with alpha and beta emitters than when we are dealing with gamma emitters.

Then, finally, another difference between I-131 and radioimmunotherapy is the fact that, again, I-131 is given orally; radioimmunotherapy is given intravenously. What are the consequences from an injection that, instead of being administered

through a vein, is administered through an artery? What are the consequences of an infiltration of the radioactivity? By that, I mean injecting into the soft tissues surrounding the vein where that material was due to or supposed to be injected. Those are complications. Those are issues that are unique to injectable materials that are not issues that have to be dealt with orally-administered materials such as iodine-131.

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So, with respect to the Subcommittee's first charge on training and experience requirements to determine if the current requirement places hardship on the patient community, after examining all of the facts, the Subcommittee came to the conclusion that the lack of use or the infrequent use of these agents is not due exclusively to or primarily due to a lack of Authorized Users. Given all of the potential issues raised by changing these requirements, the Subcommittee recommends no change in training and experience requirements at this time.

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With respect to Charge 2, establish recommendation for the total of hours of training and experience, here the Subcommittee unanimously agreed that it is time for a thorough review of training and experience. Why? Because it has been nearly 15 years since the last review was conducted. There are new radiopharmaceuticals that are available.

For example, radium dichloride, also known as Xofigo, the first alpha emitter available for treatment of metastatic prostate

carcinoma; lutetium-177, DOTATATE, another agent that we anticipate will be available in the not-too-distant future. So, these agents weren't available 15 years ago.

Finally, equally important is the new educational paradigm, the focus on education, certainly medical education, but education in general is no longer prescriptive based on "X" number of hours, "X" number of experiences. Rather, it is based on competency.

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So, the Subcommittee's recommendation with respect to Charge 2 was to establish a standing subcommittee of the ACMUI to periodically review training and experience requirements that are currently in effect, making recommendations for changes in these requirements as warranted. In fact, the Subcommittee was established this past month.

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The report and its recommendations were unanimously approved by the full ACMUI Committee on March 10th of this year.

Thank you.

At this point, I would turn the microphone over to Mr. Steven Mattmuller, nuclear pharmacist.

MR. MATTMULLER: Good morning.

I'm Steve Mattmuller, the nuclear pharmacist on ACMUI, and I will be presenting the highlights of our Subcommittee's Report on the Decommissioning Funding Plan Requirements for the Medical Use of Germanium-68/Gallium-68 Generators.

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These two images are of the same patient. They demonstrate why there is such great interest in gallium radiopharmaceuticals. It is a patient with a neuroendocrine tumor, and you really don't have to be a physician to see the advantages of imaging with a Positron Emission Tomography radionuclide, a PET radionuclide. The image has greater resolution. That leads to greater specificity, sensitivity, and accuracy. There is the added advantage of convenience to the patient. The gallium image only takes one day to image; whereas, the older agent with indium takes two days. Another plus is that there is a lower radiation exposure to the patient with the gallium agent.

As a new drug on the very near horizon, the FDA is also involved. A company called AAA, Advanced Accelerator Applications, has already submitted a New Drug Application, or NDA, to the FDA for a gallium agent for NET patients. The FDA, realizing the importance of these agents for these patients, has given it a priority review status and is expected to approve this agent within the next few months.

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At the tip of the iceberg are the gallium agents for the NET tumor patients, as they are on the verge of clinical use here in the U.S. But lurking underneath the surface, there is a gallium agent under investigation right now for just about every tumor type.

And this interest in gallium is driven by its three advantages. One, it is a PET radionuclide. Two, it is produced by a

generator, a simple generator, versus a cyclotron. Three, the relative ease of converting a gallium diagnostic agent to a therapeutic agent.

Prostate is emphasized here as one we currently do not have a good widely-available imaging agent for prostate patients. Two, it affects a large patient population.

In regards to therapy, by replacing the gallium radionuclide from the diagnostic agent with a beta-emitting radionuclide, the new agent will retain the specificity for the tumor of the original diagnostic agent, but now it carries a beta-emitting radionuclide that can treat the tumor.

This same company, AAA, will soon file an NDA to the FDA for their lutetium-177 therapy agent for neuroendocrine tumor patients. They also have in the works a lutetium177 therapy agent for prostate patients. So, these new therapeutic radiopharmaceuticals are on the near horizon also.

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The gallium generator is a simple device that serves as a source for the gallium radionuclide. It operates in a very similar manner to those of the technetium and rubidium generators that are in use today. It has no moving parts.

The parent radionuclide, germanium, is on the column and it decays to its daughter radionuclide gallium. The gallium is removed from the generator by diluting it with a dilute HCl solution. Of the two radionuclides, only the gallium is soluble in the HCl solution. So, only the gallium is removed from the generator while the germanium stays on the column.

So, this is what we are talking about. This is a demo.

(Laughter.)

Not to worry, I am not going to try to convert you all into radiopharmacists by the end of the day.

This is the first gallium generator manufactured in accordance with a Drug Master File. DMF is an FDA term. Again, the FDA has committed to the priority status of these gallium agents, as it has already inspected the production facility for this generator in Germany.

And disposal is simple, as, basically, one puts it in a box and ships it back to the manufacturer. This is the very same method that is used in the U.S. right now every week for several hundred expired technetium and rubidium generators. For a licensee, this is, by far and away, the easiest and simplest way to dispose of a generator. It is the same method that we use for this generator. It will be put in a box and shipped back to the manufacturer.

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Okay. So, this is our regulatory issue. That is, the DFP is triggered by the derived default value for unlisted radionuclides. Unfortunately for us, germanium-68 is not listed in Appendix B of Part 30. So, its calculated trigger level is 10 millicuries, and 10 millicuries is too low for this generator.

To prepare a DFP, it is a very extensive and expensive project. And this quote comes from John Keklak, the RSO at Thomas Jefferson University Hospitals in Philadelphia, where at their facility they tried to prepare a DFP for their facility and in the end decided it was

going to be too expensive for them. So, they decided not to get a fresh generator that would allow them to use the agent in patients. They went for, in essence, an expired generator that is less than 10 millicuries, so they wouldn't need a DFP. But, then, they were only able to do investigational work in animals.

Likewise, for my facility in Kettering, Ohio, we would have similar issues, because the DFP covers not just the one area that the generator is used in; it covers all areas of radioactive material use within the license. At my facility we have 10 areas of use in seven separate buildings in the Kettering area. So, that is how it sort of mushrooms into this extensive and expensive proposition.

We are seeing the negative effects of a DFP now, as in the U.S. there are only seven active sites for neuroendocrine tumor patients.

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To further measure the effect of the DFP, the Subcommittee reached out to commercial nuclear pharmacies, and Triad Isotopes responded. Our report has their full statement. This is perhaps the most important, in that every patient in need would not have equal access to these radiopharmaceuticals, most especially those in smaller and more rural markets.

This statement from Triad does have added substance and significance, as they have a DFP in place at four of their facilities now that operate the cyclotrons. Hence, they have firsthand knowledge and experience as to how extensive and expensive a DFP can be.

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So, we are quite certain that the cost of a decommissioning of a medical use gallium generator does not warrant the need of a DFP. We do know that the current DFP requirements have already and will continue to limit patient access to gallium's use.

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From our Subcommittee report, this was our proposal of creating a labeling value of 10 microcuries in the Appendix. We have two reasons why we believe we are on solid for this.

First, the 10 microcuries. Dr. Langhorst of our Committee dug into the Law Library at Washington University and found all The Federal Register notices referenced in Appendix B. From those notices, she found the actual methodology that the NRC used when it first calculated the labeling values for radionuclides in this Appendix. By using this same methodology, she calculated a value of 10 microcuries. That would, then, correspond to a 1,000-millicurie trigger limit for a DFP. We have extra confidence in her calculations in that this is the very same label quantity the NRC calculated for germanium-68 when it revised Appendix C to Part 20 in 1994.

In addition to this, secondly, if you consider the actual decommissioning issues for the germanium in the generator -- I mean, it is practically a sealed source -- I think you have to conclude they are minimal, as to dispose of the generator, simply you put it in the box and ship it back to the manufacturer. This proposed relief would allow licensees to use the gallium generator without the burden of a DFP.

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So, yes, the NRC is tasked with ensuring the safe use of radioactive materials in patients, but we also have a responsibility to maintain a proper balance and not to be a barrier.

These three neuroendocrine tumor patients are an important reminder of why our Committee exists and why we are here today. They are holding placards that state the number of years that it took them to get an accurate diagnosis for their disease. For these patients, unfortunately, it takes them three to seven years to get an accurate diagnosis. This, of course, desperately needs to be improved, as, sadly, when most of these do finally get their correct diagnosis, their disease has progressed extensively.

So, yes, these patients deserve our attention. The FDA is on track. They have given priority review to the gallium diagnostic agent. They have been to Germany to review the production of this. You have seen our initial proposal, and we are very encouraged that staff is working on an exemption and, then, the procedures for a direct final rule for relief. So, we are very encouraged and hopeful that the NRC will soon bring these two efforts to fruition for the benefit of these patients.

Thank you.

DR. ALDERSON: Hello again.

I will close out our presentations today by addressing the important topic of communications. I will suggest ways by which the NRC staff could enhance communications with the ACMUI, as well as how the ACMUI can help enhance the NRC's relationship and communications with the medical community. Before I begin, I would

like to state that the ACMUI feels that our current communications with staff are really quite good, but there is always room for improvement.

Next slide, please.

The ACMUI is a federal advisory committee that reports directly to the Director of the Division of Material Safety's states, tribal, and rulemaking programs within the Office of Nuclear Material Safety and Safeguards. The day-to-day activities of the ACMUI are supported by the Medical Safety and Events Assessment Branch.

Next slide, please.

Now this is simply a chart, a table of our organization to display our communication pathways. The dotted lines indicate our availability to speak with the Office of the Director of NMSS, with the Executive Director of Operations, and with, of course, the Commission. Our immediate past ACMUI Chairman was able to meet with all the individuals in this chain during the last fall ACMUI meeting.

Now we will review current communications.

Next slide, please.

The ACMUI meets at NRC Headquarters twice each year, holds multiple ad-hoc teleconferences, and meets with the Commission on an annual basis. The ACMUI Coordinator is the primary conduit for transmitting and receiving communications.

Next slide, please.

The ACMUI informs the NRC staff about emerging medical issues, and NRC seeks input from ACMUI on medically-related topics, including rulemaking and licensing actions.

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For various items, through NMSS Policy and Procedure 2-5, the ACMUI is provided with 60 tp 90 days for review and comments.

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So, the ACMUI produces subcommittee reports which provide recommendations on various topics. The ACMUI's unfettered opinions are captured in papers to the Commission. But the question is, then what?

Next slide, please.

Now this slide is relatively brief, but the comments are relatively extensive. So, I wanted to warn you about that before I proceeded with these comments.

So, per NMSS Policy and Procedure 2-5, the ACMUI's opinions in the form of that final Committee report are included in papers to the Commission for items that are pertinent for the Commission. At other times, the Committee's reports are reviewed and evaluated for other non-rulemaking activities such as licensing guidance documents.

The standard process is that staff transmits a memorandum to the Committee within 30 days after a meeting to capture the recommendations that the ACMUI has made. Staff also recaps recommendations from previous ACMUI meetings during our spring and fall meetings and notes if any actions or changes have been taken.

Now comes the suggestion for ways to potentially improve. A way to improve our communications with the staff would

be if staff would provide us with additional feedback as to why a recommendation made by the ACMUI was not accepted or why no action was being taken.

This particular issue was recognized during the recent OIG audit of the NRC's Medical Program. As a result of that audit finding, the staff has committed to transmitting formal feedback to the ACMUI with detailed explanations and responses to our recommendations. I think I speak for the whole ACMUI when I say that I think this is an excellent action from the staff.

Next slide, please.

Now our Committee's main objective is to provide the staff with advice as it is related to medically-related topics. In order for us to provide the best recommendations possible, the staff should give the Committee an overview of the internal processes and regulatory tools that are available to us. So, as per my conversations with staff during the fall 2015 ACMUI meeting, counsel from the Office of the General Counsel will begin giving us such training during tomorrow's closed sessions. And thank you to Ms. Esther Houseman for addressing the Committee's needs in this way.

Next slide, please.

All of the members on this Committee are members in other professional societies and organizations within the medical community. As NRC seeks to improve their relationships and outreach with the medical community, the ACMUI can serve as a conduit of information. Members, along with NRC staff, could speak at major society meetings. This could also shed light as to the role that

the ACMUI has with the NRC staff and improve the understanding of the society members.

Well, thank you for listening to our recommendations. This concludes the formal part of our report, and we are now available for questions and answers.

CHAIRMAN BURNS: Thank you, Dr. Alderson, and thank you all for the presentations.

We will begin questions this morning with Commissioner Ostendorff.

COMMISSIONER OSTENDORFF: Thank you all for being here and for your service on the Committee. It is of tremendous importance to the agency staff and the Commission, because we do not practice medicine, that we have your upfront experience-based, professional-based insights into these critical issues. So, thank you.

I am going to start out with your last presentation, Dr. Alderson. I read between the lines maybe some frustration with the NRC, but I appreciate the professional way in which you presented your comments. It was very objective. I wanted to maybe just make a couple of comments and maybe ask you a few questions.

DR. ALDERSON: Sure.

COMMISSIONER OSTENDORFF: Certainly, the Committee members, it is always our intent as a Commission that the Committee understands the decisions by the Commission, recommendations by the staff, et cetera. So, this agency is extremely open and transparent, and nobody is trying to play hide the ball.

So, I think what we are sensing from your presentation

is that perhaps we can improve in that area. Certainly, you deal with such difficult issues across your communities, within your communities, that it should not be made more difficult by lack of understanding of how we regulate. And so, I appreciate your raising the topic.

I think you know that we all have open-door policies. You can come by. I know you have very busy professional schedules, treating patients, doing your normal day jobs, but I would welcome the opportunity -- and I think I speak for all my colleagues -- to have members come by and see individual Commissioners to discuss any particular issues.

I think you know all of our votes on our website. So, when we deal with an issue that touches on the Committee's substantive expertise, the votes we have area all made public. Hopefully, our staff is giving you some feedback on those votes. Is that happening?

DR. ALDERSON: Yes. Yes, it is.

COMMISSIONER OSTENDORFF: Good.

DR. ALDERSON: The reason that we are pursuing all this wide range of communication is because, yes, we bring medical expertise and advice. We don't necessarily have all the familiarity with the agency's organization and approaches, and perhaps even the agency's vocabulary and acronyms that we should have. And so, what we are really asking Ms. Houseman to do tomorrow is to go through with us some of the very basics that the people who work here every day and all of you probably understand quite well that we might not understand completely. Through learning about that, we can be better

informed about the recommendations we can make and how we can pursue them appropriately within the agency.

COMMISSIONER OSTENDORFF: And I applaud the Committee and OGC for facilitating those discussions. I think they are very important.

Just are there any particular Commission decisions that have troubled the Committee or that have created "Well, what the heck is going on here" kind of reaction? I think we would be interested in hearing that.

DR. ALDERSON: No, I don't think that is the case. I think it is more that, as the ACMUI, the experts would discuss a particular issue, one particular person would say, "Well, we can go do a guidance" and someone else could say, "We could go here." And it was clear that different members of the ACMUI didn't fully understand what was available to them, and that it would be very useful to us to have some education in that regard. So, that is why we asked for it.

COMMISSIONER OSTENDORFF: Okay. Well, I really appreciate you in your role as Chairman bringing this up to the Commission. I think this was very important.

DR. ALDERSON: Thank you.

COMMISSIONER OSTENDORFF: So, thank you. I know that it is not anyone's intent for there to be anything other than fully-open and transparent interactions and explanations. I appreciate Esther's meeting with you all.

I am going to Dr. Zanzonico. Did I pronounce that correctly?

DR. ZANZONICO: Correct.

COMMISSIONER OSTENDORFF: Yes, okay.

I have not been here quite as long as my good friend and colleague Commissioner Svinicki, but I have been here six years. This is the first time -- and I appreciate the different opinion you provided us -- the first time I have been to the Commission meeting where there has been a suggestion that we tailor back or eliminate some of our website or information provided to the public. So, your presentation really got my attention.

I think one of the values of having a Commission meeting is for us to be able to hear different views, even if they disagree with the direction that we have previously provided to our staff.

So, I guess I wanted to maybe get into some of your presentation from the standpoint of the original intent, I think, and Laura has been a key player in this for many years in helping advise us on the patient advocacy side of the house. I think our original intent of this website was to provide what we think is our regulatory responsibility to the public to communicate in those limited areas within the use of radionuclides, radiopharmaceuticals to the public as to what our regulatory footprint is.

I believe in the iodine-131 arena, that has been around ever since I got here in 2010; we have had many meetings on this topic, whether it be -- well, we have had a lot of meetings. I will just put it that way. And we have had lots of input, lots of letters to the Commission from many people across the United States, from Congress, and so forth.

So, it really got my attention when you were suggesting that we should not be communicating in that. I think one of the original intents of the Commission and the staff was we were not seeing consistent information being communicated by the medical community to patients. I realize we are not part of the patient/physician relationship, but I think the intent was well-intentioned when it was directed a few years back, which was, hey, we are seeing an uneven practice by physicians through examples brought to the agency as to how some of these issues were being communicated.

Now, having said that -- and you may agree or disagree -- I guess one thing was that some of the information we are putting out is inaccurate or misleading?

DR. ZANZONICO: No, not at all. I was not questioning at all the scientific rigor or correctness --

COMMISSIONER OSTENDORFF: Okay.

DR. ZANZONICO: -- of what the NRC staff is compiling. We actually haven't seen that in detail at the moment. But, knowing the people involved and just knowing the quality of work they produce, I have no doubt that what ultimately will appear will be scientifically-sound. That is not a concern.

COMMISSIONER OSTENDORFF: I remember six years ago in a visit I made to the University of Pittsburgh Medical Center looking at these issues and actually seeing the instructions for patient release, and talking to our Region I staff in Pennsylvania and our staff here, I had a very small sample set. So, I am not suggesting I did a full-scale survey. But there appeared to be some variability in the

practice of how some of these issues were communicated to patients. And I think that was probably the main driver for what we are trying to achieve.

I want to stop right there, just because I appreciate your raising it because it is a little different from what we typically hear. And that is a good thing, for us to have differing opinions, even if they disagree with prior direction that we have provided to our staff.

Laura, do you want to comment any in this area? I know you made a statement earlier, but --

MS. WEIL: Again?

COMMISSIONER OSTENDORFF: But I will give you the opportunity if you want to. I know you have already commented on it, but --

MS. WEIL: No, I think the portal is going to be extremely useful, in that it is going to bring up the discrepancies in information that patients receive. Also, it will raise the issue because patients will communicate as well their frustration with a lack of information that they are receiving, which just shows that there is a lack of consistency across this issue in the way patient care is provided.

COMMISSIONER OSTENDORFF: Thank you.

DR. ZANZONICO: If I may just follow up?

COMMISSIONER OSTENDORFF: Please. Absolutely, yes.

DR. ZANZONICO: There is no disputing that there is inconsistency, lack of uniformity, however you want to characterize it, in the instructions and information that is conveyed from treating

physicians to their patients.

The concern I have, and at least some of the members of the Committee have -- and I think physicians have encountered this not just in context, but in others where a patient comes in and says, "But the internet says this."

COMMISSIONER OSTENDORFF: Yes.

DR. ZANZONICO: And, of course, we know everything on the internet is accurate.

But that is the real concern, that we think that the appropriate line of communication in the entire scope of patient care is directly from the physician and allied health professionals --

COMMISSIONER OSTENDORFF: Yes.

DR. ZANZONICO: -- to the patient. The concern is that a website with the imprimatur of the NRC may convey information that is generally accurate, but, for example, may not be appropriate in a particular patient's case. And now, the patient confronts the physician -- "confront" is probably not the right word -- saying, "The NRC recommends or says this. You're telling me this. What's correct? What's true?" and so forth.

So, that is the concern, that no website, no matter how credible, no matter how scientifically-sound, can address all of the vagaries in patient care and really substitute for the physician who has firsthand knowledge, obviously, of the patient situation. It is this potential for conflict that, as I said, I feel may exacerbate anxiety and confusion among patients.

COMMISSIONER OSTENDORFF: Okay.

DR. ZANZONICO: So, that is my concern.

COMMISSIONER OSTENDORFF: I think I probably have a different view, but I respect your view. I'm not a physician; you are. I know that when I have gone through a major surgery procedure here and have gone through cancer treatment myself, I found a lot of benefit in being able to go to a website.

I don't know that The New England Journal of Medicine, which I did go to for several of my research efforts for cancer treatment for myself -- I struggled a little bit to figure out where the best information was.

And so, I will leave it at that. I just appreciate your raising the issue today. Thank you all.

CHAIRMAN BURNS: Thank you, Commissioner.

Commissioner Baran?

COMMISSIONER BARAN: Thanks. Well, thank you all for being here and for your work and your presentations today.

Dr. Palestro, I want to start with some questions focused on the alpha and beta emitters question and the training and education requirements there.

I looked at the Subcommittee report that came up, and it didn't really discuss the relative risks to patients or to the public of alpha and beta emitters generally as compared to gamma emitters or iodine-131. You talked a little bit about that today, actually, in your presentation, but I was hoping to hear a little bit more about that.

You know, compared to gamma emitters or iodine-131, are beta emitters generally lower risk to the patients and are they lower

risk to the public, or is that not the case?

DR. PALESTRO: Well, I think that is a difficult question to answer because, as I at least tried to indicate in the slides, they are really very different. If we talk about misadministration in terms of amount of administered activity, I think it would be hard to argue that one is more or less hazardous to the patient. If we gave twice the amount of radioactive iodine, and let's talk about thyroid cancer as opposed to hyperthyroidism, certainly, the potential side effects in terms of myelosuppression, lowering blood counts are potentially there; equally so with alpha and beta emitters. So, there I would say that the risks are comparable.

COMMISSIONER BARAN: You talked a little bit about spill issues.

DR. PALESTRO: Yes.

COMMISSIONER BARAN: What about more broadly in terms of risks to the public, in terms of folks being released and those types of issues that come up in iodine --

DR. PALESTRO: The answer is certainly with I-131, because of the more energetic photons that are emitted, there is a greater risk of exposure to the public. We are assuming now that everything has been administered correctly and we are putting misadministration aside.

On the other hand, alpha and beta emitters travel a much shorter distance. So, exposure to the public or risks to the public are going to be less.

COMMISSIONER BARAN: Okay. But, going back

to misadministration, what I am hearing is, if the question is misadministration, alpha and beta emitters have comparable risks to gamma and iodine?

DR. PALESTRO: In terms of if we are talking about misadministration, excess amount of activity administered.

COMMISSIONER BARAN: Okay.

DR. PALESTRO: On the other hand, if we are talking about a misadministration where we have the leakage of the dose into the surrounding soft tissues or an intra-arterial injection as opposed to intravenous, that is unique to any injectable radiopharmaceutical. It is not going to happen with iodine-131 because that is administered only orally.

COMMISSIONER BARAN: Okay. So, there is no simple, clear answer to this question about, well, this is lower risk than this other thing? I mean, if you are looking at categories, alpha, beta, gamma, iodine, if we break out separately, it is kind of complex?

DR. PALESTRO: I think that is an accurate way to characterize it, that it is a complex issue, and each of these agents has their own set of risks that in some circumstances are unique to them.

COMMISSIONER BARAN: Okay. So, right now, of course, the regulatory construct we have here is there is one training and experience requirement of 700 hours for using the full spectrum of nuclear medicine. I think, based on all the letters we are getting and the conversations that we are hearing, there is this, I guess, policy question about whether or not, as an agency, we should explore having more tailored training and education requirements for certain classes of

radiopharmaceuticals. Is that something that you all have talked about in the Subcommittee or Committee? What are your thoughts about that type of approach and how complicated do you think it would be to do that?

DR. PALESTRO: The answer is the purpose of the Subcommittee that has been formed, the new Subcommittee, is specifically to look at that issue.

COMMISSIONER BARAN: Okay.

DR. PALESTRO: Should it be a unified set of training and experience requirements? Should it be divided by category? In fact, one of the letters we received from Hilliard, et al., suggested that the training and experience and authorization for use be limited to specific radiopharmaceuticals as opposed to classes of radiopharmaceuticals.

So, the answer is it is a very complex issue. I think it does need to be looked at extensively, and I think that it is something that takes time. It is just not something that can be accomplished in a matter of weeks or months. I think it has to be looked at over time. Figure out what exactly we mean by competency, and then, work backwards. Once we have said this is what we expect the Authorized User to be capable of doing, determine, so to speak, in a retrograde fashion what sort of training and experience are involved, without getting into preconceived notions about numbers of hours and numbers of actual cases that qualify for experience.

COMMISSIONER BARAN: Okay. And understanding that you all are just starting to look at this, at this stage

do you have kind of an intuition about, if we were going to take a category approach, classes of radiopharmaceuticals, do you have a sense about the number of classes we would be talking about? Is it going to be alpha, beta, gamma, iodine or is it going to be more complicated than that likely?

DR. PALESTRO: I think it would be injectable alpha and beta emitters and, then, orally-administered radiopharmaceuticals, which in this case is I-131.

COMMISSIONER BARAN: Okay.

DR. PALESTRO: It is difficult to really look that far into the future --

COMMISSIONER BARAN: Yes.

DR. PALESTRO: -- because that is what we are dealing with at the moment. But I would think we would be focusing on classes. Specific radiopharmaceuticals in one sense is kind of interesting, but I think it also may become overly-burdensome and unnecessarily and excessively regulated. But, again, that is just sort of a preliminary thought of my own.

COMMISSIONER BARAN: Yes.

DR. PALESTRO: And the Subcommittee hasn't looked at it in-depth.

COMMISSIONER BARAN: What do you think, as you embark on this, what kind of level of effort is going to be necessary to develop the safety case for any particular training and education requirement for any particular potential class of drugs?

DR. PALESTRO: I think the initial development for

one class -- we will just focus on one class --

COMMISSIONER BARAN: Yes.

DR. PALESTRO: -- will be fairly difficult and comprehensive and will take a lot of vetting. I think once it is established for one class, we will have a template for other classes.

COMMISSIONER BARAN: Okay. And you mentioned and the Subcommittee report discussed a little bit about this shift in education to something that is more kind of competence-based as opposed to precise hours. Again, I know this is something you will be looking at as part of the new Subcommittee.

But talk to us a little bit about what do you see as the potential implications for NRC's role of looking at more of a competence-based approach? What is that going to look like? Are we talking about a situation now where NRC has exams for doctors on radiological safety? I mean, it seems at least at a conceptual level in tension with the idea that we are not going to get involved in the practice of medicine, to judge whether an individual doctor has the competency to do something safely.

DR. PALESTRO: That is really looking far into the future. But, certainly, one of the ways that competency is judged is by examination. Competency really isn't measured exclusively by "X" number of experiences; for example, three administrations of a particular radiopharmaceutical. That may be competent for some individuals. It may be more than enough for others. It may be nowhere near enough for still other individuals.

So, there has to be some measure of competency.

While I am not suggesting, and I don't think the Subcommittee is going to suggest, that the NRC develop examinations, there is, in fact, a precedent that was set by the American Board of Endocrinology where they have the Certification Board in Nuclear Endocrinology, in which they have developed a program for training and experience, at the end of which the individuals who must be Board-certified in endocrinology take an examination. Once they are certified by the Certification Board in Nuclear Endocrinology, those credentials are accepted by the NRC for Authorized User status.

So, that might be, ultimately, what I personally -- and I am not speaking for the Subcommittee or the ACMUI -- personally might envision, the establishment of some sort of certification board that would give the NRC confidence that these individuals are, in fact, qualified to administer these agents.

COMMISSIONER BARAN: Okay. Thank you.

DR. ALDERSON: Dr. Alderson here. I would like to just comment on that because I have thought about that. I thought Dr. Palestro's answer was actually quite good.

But I don't personally see -- again, now speaking as myself and not for the Committee overall -- that we would ever get involved in testing. But if we had ideas about what defined competency or the capability to be safe, you could virtually issue an RFP and go out and try to find people or organizations that would say, "Well, we could do this for you." We could do it in such a way that we could establish the qualifications and periodically review those qualifications in a certain way. Then, that might be sort of a decision

approach that you could make.

Part of what I think we are dealing with here, I think that many of the things we have discussed in the last few minutes have to do with sort of the education-versus-regulation question, which is a difficult balance. I think they do exist on a continuum. So, we have to work with you to try to find the right balance for communication, which is a form of education, down to when does it become regulation and how do you stay away from getting parts of the community concerned that there is too much regulation. I think more education will help with regulation and, ultimately, help with safety. So, it is going to be an ongoing process, and we are very interested in getting started.

COMMISSIONER BARAN: Thanks.

I wanted to ask Mr. Mattmuller just one quick question on the germanium/gallium generator issues. So, I take your comments, your view is that a decommissioning funding plan isn't necessary because decommissioning is very easy. It just returns to the manufacturer.

My question on that is just, is the manufacturer contractually or otherwise legally obligated to take back from the licensee the generators at the end of their useful life?

MR. MATTMULLER: This generator is manufactured by Eckert & Ziegler, a German company. I believe there is a second generator company called ITG that is on the verge of also having their DMF approved by the FDA. Both of those companies are in Germany. By German law, they are required to take back any gallium generators that they produce.

COMMISSIONER BARAN: Okay. Thank you. Thanks again.

CHAIRMAN BURNS: Thank you, and thank you all for your presentations.

I want to come back to the germanium generators. But just to reflect on some of the discussion we have been having on this education requirement, I think Dr. Alderson's comment is very interesting, this intersection between regulation and education. In fact, what we have now is regulation that says education must be 700 hours. And so, the question, and I think what we are getting on this side, is a lot of letters saying, "Is that really the case? Is that the necessity of education in terms of safe use, safe administration of radiopharmaceuticals?" So, I think we will all be very interested as this goes on in terms of the Subcommittee about where that balance is and where the interplay finally comes.

Dr. Palestro, what do you foresee in terms of sort of a course of work for the Subcommittee on this question, on the educational requirements? What sort of planning? I realize you can't plot out perhaps a particular endpoint, but just sort of give me some flavor of where you see them, where you see you all going as to this.

DR. PALESTRO: Well, I think the first thing we need to do is determine the various boards that have the so-called deemed status by the NRC, figure out and determine where those Authorized Users are coming from, just so you have some sort of baseline. I think that is important.

Then, I think we need to look at what we deem as the

requirements for an individual to be competent as an Authorized User. What do they need to be familiar with, handling the radiopharmaceuticals administration of radiopharmaceuticals, radiation safety, items like that?

And then, finally, we also need to try to determine what constitutes competency in those areas. From that point, I would think we would work backward to hours and experience. In other words, start out with competency and, then, try to determine -- and I don't think it is an easy task -- but try to determine what amount of hours and experience is required, because there is always going to be some minimum that is required.

I think -- and again, I am going to speak for myself and not for the Subcommittee or the entire ACMUI -- given the excellent track record in terms of safety that the current requirements of 700 hours have for training and experience, we are not going to recommend an increase in those hours at all. But whether or not we recommend a decrease I don't know yet.

CHAIRMAN BURNS: Okay. And help me out, just to refresh my recollection. The current 700, it is a mixture of classroom and, then, doing the medical --

DR. PALESTRO: Yes, it is, I believe, 200 hours of didactic experience --

CHAIRMAN BURNS: Okay.

DR. PALESTRO: -- with 500 hours of, quote/unquote, "clinical experience".

CHAIRMAN BURNS: Okay.

DR. PALESTRO: Eluting generators, preparing radiopharmaceuticals, so forth.

CHAIRMAN BURNS: Yes. Okay. I think I have an hour in. I visited Inova Fairfax, and they had me doing a couple of things. It was actually very interesting a couple of weeks ago. I have a greater respect for those who actually have qualified and are doing it, demonstrating, for example, a seed implant for prostate cancer and one of the others. But I am nowhere near qualified.

I want to talk, Mr. Mattmuller, about -- and you may have answered my question in response to Commissioner Baran -- but, with respect to the generators, I think what you said is, currently, basically, the manufacturer -- or these generators are coming from Germany. It is an import from Germany. I think what you said is, under German law, basically, they have the responsibility -- because one of my questions was, how does Germany treat the disposition of these? I think what I heard you say was, basically, under the German law, that the manufacturers are required to take back. So, they are responsible for the ultimate decommissioning and disposal, et cetera.

I take it in a way, because, for all I know, at some point there might be an American company, a Canadian company, or others who might be interested, it seems to me that I think what you are saying is that, if you have -- again, with licensed material, whether it is in the medical area, whether it is reactor fuel, whether it is radiography device, or whatever, the whole question is responsibility for possession, while in possession, responsible for the appropriate use, licensed use, and control, and ultimate disposition.

So, what I think I hear you saying, if there is an assurance in the system -- and that might be demonstration through contract or some other means -- that, basically, the hospital or the user has a right to return, and the manufacturer or the supplier has an obligation to return. That seems to be almost the linchpin or the key piece that would help, from your standpoint, this notion of either an exemption or an exception in the rule. Do I have that right? And then, please elaborate.

MR. MATTMULLER: Yes, sure. You said "the right to return". Actually, for this generator, and just to back up, and maybe I can bore you a little bit more about the other generators, in regards to technetium generators, especially the large ones that have the depleted uranium shield, if you use that generator, you are required to send it back to the manufacturer, primarily because of the expense of the shield.

For a rubidium generator, because of the long half-life of the parent radionuclide strontium-82, it is impractical for a site/a licensee to dispose of that onsite by decay in storage. So, that is recognized by the current manufacturer, Bracco. So, they, too, require those generators to be sent back to them for proper disposal.

So, this really fits into that same pattern. It is not that we -- I guess you can say we do have a right, but it is almost like we are required to send it back to the manufacturer for disposal. In this day and age purchase agreements, and they used to be this big when I first started, and now they are several pages. But, of course, for this generator, there is a full page -- or I shouldn't say a "full page" -- but

there is a specific clause on the return of the generator when it is expired back to the manufacturer.

CHAIRMAN BURNS: Okay. So, it does seem to me that, as I say, you indicated an interesting sort of developmental history here between the last revision, Part 20, in the early nineties; also, Part 30 in terms of how some of the exemptions and quantities are stated. Sort of an interesting development.

But, again, it does seem to me that seems to be the linchpin or the strongest argument perhaps or a strong argument for allowance of an exemption or some similar regulatory device that Ms. Houseman will explain more about tomorrow, apparently. That might provide the basis for such an exemption.

Okay. I wanted to follow up on some comments Commissioner Ostendorff made with respect to I think the staff's initiative in terms of looking sort of at this website communication. I think it is recognized that we are in a day and age where you are going to have information out there.

To the extent that we provide information out there, we have to make sure, I think, it is accurate. When I took a look at what I think is this sort of experimental, if you will, site now, perhaps some of what might be more useful on it is if it does address some of the concern that you have in terms of the question of practice of medicine, that you need consultation with the physician, consultation with the expert is something that may need to be emphasized.

On the other hand, what I see is references to various societies, other expert panels where other information is. And maybe

it is the contexting that could be improved.

Either Ms. Weil or Dr. Zanzonico can comment on that.

DR. ZANZONICO: Well, I would hope that, at the very least, there would be a very emphatic statement on any such website that, as with other educational materials created generally, that it does not substitute for information, advice, recommendations, and so forth, by the patient's physician. I think that is a minimum standard for any informational mechanism.

Beyond that, until there is a draft site, and so forth, available for review, it is difficult to comment on the specifics.

CHAIRMAN BURNS: Okay.

DR. ZANZONICO: My comments were really more philosophical --

CHAIRMAN BURNS: Okay.

DR. ZANZONICO: -- than any detailed assessment of what might or might not be on a site, but certainly a disclaimer emphasizing the primary role of the physician/patient relationship I think would be a minimum requirement.

CHAIRMAN BURNS: Okay. Thanks.

Ms. Weil?

MS. WEIL: I think something that the site has already demonstrated is that there is a surprising unknown percentage of patients who get very little to no information about release instructions from their physicians. This is a method of promoting from the patient side a conversation with the physician to get the information that they need, which will be of benefit to everyone.

CHAIRMAN BURNS: Okay. Thank you.

My time is up. Commissioner Svinicki?

COMMISSIONER SVINICKI: Thank you all again. Let me begin by expressing in the most heartfelt way that I can my gratitude for the work of the Committee, not just the members who presented at the table today. I know a number of other Committee members are here sitting in the audience.

It is my observation that the NRC's regulation of some of these medical issues is not always the most comfortable fit with the remainder of our regulatory framework, partly because the issues are different in many ways than what we regulate in other areas of our regulatory framework.

My confidence would be lessened, I think, quite a bit in the appropriateness and correctness of our regulatory outcomes, but for the existence of your Committee. Your Committee does report to the NRC staff. I consider that is just one of the vagaries of advisory committee law and regulation, unlike our Advisory Committee on Reactor Safeguards, which is in the Atomic Energy Act.

I view it also as a strength because it is a little bit of a workaround, but I think the strength of the ACMUI is it is absolutely essential that we have current practitioners who are out in the field, again, working directly on these issues. It is a very dynamic area of medical technology. I think that if we had to have retired individuals and others, so that they would have maybe less direct interest in the regulatory outcomes, I think that we would suffer from having individuals who were not as contemporary on these issues in medical

settings.

And so, I view the fact that the ACMUI does not advise the Commission directly or its recommendations do not flow directly to the Commission, it certainly in no way is reflective in my observation of the significance of the Committee's work product. Every member of this Commission I have ever served with, including the present company, gives very heavy weight to the Committee's input and recommendations.

We may occasionally arrive at a decision that is a modification or a departure from what you recommend. At our level as Commissioners, we have broad other public policy and regulatory and legal considerations. So, sometimes we have a balancing of factors and that may modify the Committee's input. I appreciate your recognition of that here today. I feel that in a number of your responses there was recognition of that.

And certainly, the reporting which was in one of the early charts, the reporting scheme is not in any way reflective, in my view, of the degree of importance of your work very directly to the lives of American people every day, which is a very, very direct connection between your expertise and advice to our regulatory processes.

So, I just wanted to take a moment to express that to each of you. I am sure it is very difficult to balance your other work with your service on this Committee. I appreciate that you all do that. In my experience over, yes, Commissioner Ostendorff, a very long number of years, all members of the Committee serving and previous members do that very well. And I am very grateful for it, as a member.

As a decisionmaker, these are tough decisions for us. Again, I reside a lot of confidence in the existence of the ACMUI, and they are playing a role in these decisions, not always the decider, but playing a very important role in the decisions.

So, I will turn to communications. I have talked about the reporting chain. I think I don't want to beat the Patient Release Project website to death because we have talked a lot about it.

Dr. Zanzonico, your comments were not at all surprising to me. I just need to take a moment to remind us all of how the Commission came to direct the NRC staff to develop that website. It was not the NRC staff's recommendation to us, and the ACMUI broadly had expressed a number of concerns about what is a potential -- and I say just "a potential" -- intrusion or insertion of NRC between a doctor and a patient.

Two members of the Commission, including its Chairman at that time, took up a personal advocacy on this issue. And the staff was engaged in a longer-term project of assessing the circumstance and coming back to us. The Commission as a whole truncated that process by its own choosing and moved forward.

I was the sole vote disapproving moving forward at that time. I thought it was premature at best, and in the absence of full vetting by the staff and a recommendation, my concern was we might inadvertently, contrary to the adage that something is better than nothing, in the case of a bad website, I thought -- and I took the concerns to heart -- that a bad website would be worse than nothing. So, it was not the staff's recommendation. It was not the ACMUI's

recommendation.

And so, I really respect the concerns that you have expressed. Now our very capable patient advocate has also reminded us of a number of sensitivities, and I weight those heavily and those are very valid as well.

But I do think we arrived at this through something that originated with the Commission itself. I worried about this potential insertion of something.

Again, I am going to go out to the website or many websites and look for information if I am a patient. But the person who knows my case best is my medical care provider.

And so, I hope we will do it well. The staff, I don't have any doubt, even though this wasn't their idea, they are extremely professional.

What I would urge you to do is please continue to raise any issues or concerns about information we are putting out. I am not going to beat up on you about it. I think it is important.

I didn't share the view that necessarily we should do this or do this without a little more work by the staff. That decision is made. I am not relitigating that. But the most important thing now, if it is out there, is that it be something that is constructive as opposed to something that just increases patient's and loved one's anxiety about why is the NRC saying this and your doctor said something else. So, I don't want to beat up on that anymore.

I will say a lot of my colleagues have asked about the training and experience requirements. I don't know what the answers

are there, but the one thing that resonates with me is your recommendation for a broad relook, that it is time. It has been 15 years. That sounds about right.

I think I have one question there, though, for anyone who would like to answer it. What is your confidence about our ability to put in place something enduring if it takes the form of a stratified injectables versus things delivered orally or if it is based on the modality or the therapy?

The one thing I took from Dr. Palestro's presentation was how dynamic the treatment or development of therapies, diagnostics, the various modalities, that is dynamic. We don't change our regulations terribly frequently. So, do you think that we can get to something that is informed in an enduring way, that we won't have to change 500 hours to 100 hours or do that? What is your view on our prospect there?

DR. PALESTRO: You know, it is always difficult to look far into the future because we don't know everything that is developing. I would hope that the final product will be one that is both comprehensive and flexible and can encompass degrees of change. I think there are going to be changes that may be beyond what we could have envisioned, and we will deal with it when it comes. So, again, it should be comprehensive, but flexible to the extent that we can make it.

COMMISSIONER SVINICKI: And I appreciate that. Maybe the answer was a little bit unanswerable because it was asking for a crystal ball. I think more truly new things, it is hard to encompass in any regulatory proposal. But maybe what I am suggesting is, as you

approach your recommendations in this area, you are getting a sense or you will hear more tomorrow about how long our rulemaking process is. Maybe standard timeframes will be presented to you.

If you could maybe recommend with that at least a consideration. You said, you know, enduring things that encompass at least what we foresee. As far as I am concerned, that is the right mindset to move forward.

And I will just close with a comment -- I don't know if I have a question -- on the germanium/gallium generator issue. I do appreciate that presentation. I view this as ACMUI helping NRC look over the horizon or get on top of something before it becomes a big issue.

Speaking only for myself, I at this point assess that the staff is looking at the issue and perhaps drafting some sort of direct final rule or exemption. I don't know what final form that would take and what ultimately will be decided, but that work to move in that direction clearly seems appropriate to me, as an individual member of the Commission, because I think at bottom that patient image that you, Mr. Mattmuller, began your presentation with, you could just begin and end with that.

For me or my loved ones, if we could have the benefit of the imaging, that is, the difference between those two, the difference that could make in the treatment, the care of a patient to me is so telling. And I am not medically expert in anything, but, clearly, we don't want our regulatory framework to stand as an arbitrary non-safety, non-risk-related obstacle to people having broader access to that kind

of imaging.

So, I have talked a lot, but, just quickly, did anyone have anything they felt they really needed to add? If not, I will yield back, Mr. Chairman.

MR. MATTMULLER: Actually, I had a thought in regards to your comments, Chairman Burns. In regards to the contractual requirements for sending it back, I was thinking, well, what is the alternative? As you might suspect, I am old enough to remember for technetium generators we used to store them in decay for storage to dispose of them. But that required holding onto the generator, dismantling it, pulling the column out that had the parent radionuclide on it. And then, for technetium, it is a 2.8-day half-life. So, it is at least two months, and then, storing that, but, then, going back and verifying with your survey meter that, yes, indeed, the column has decayed to background. And then, you can dispose of it.

Fortunately, the manufacturers developed programs where you can either do all that extra work or it can be simpler and just send it back to us. And so, the field has evolved, especially in the case of the more expensive shields, or the rubidium generator it is a much longer half-life, or it is not practical to store the columns in your closet. It is routine, I guess, is the word I want to put out there. It is just routine. That is what we do now, yes.

CHAIRMAN BURNS: Yes. Thanks for that. Thanks for the explanation. It does tell you in terms of how, you know, the use, the technology, the market has developed in terms of how, and is developing in terms of how the devices are used and the practicalities

of how they are handled, stored, and disposed of. So, thanks for that additional thing.

Again, we appreciate the presentations by the Committee members who are at the table, but, as my colleague has said, we appreciate the service of those others who are sitting in the background there. I recognize a number of you who also serve on the Committee. We appreciate the work. As we have all indicated, I think it is extraordinarily useful in terms of informing us in terms of our general safety mission, but particularly in the area of the intersection with medical applications of radioactive material. So, again, thank you.

With that, we are adjourned.

(Whereupon, at 11:05 a.m., the meeting was adjourned.)