

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

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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 begin, 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

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

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

7 (No response.)

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

9 DR. ALDERSON: Thank you.

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

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

16 The next slide, please.

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

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

23 Next slide, please.

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

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

6 Next slide, please.

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

11 Next slide, please.

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

15 Next slide, please.

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

20 Next slide, please.

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

26 Next slide, please.

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

3                   Next slide, please.

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

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

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

12                  Could I have the first slide, please?

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

19                  The next slide, please.

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

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

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

7 Next slide, please.

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

14 Next slide, please.

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

21 Next slide, please.

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

1 patient safety issues.

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

7 Next slide, please.

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

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

18 Next slide, please.

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



1 Next slide, please.

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

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

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

25 Next slide, please.

26 And so, the inadequacy and inconsistency in radiation

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

6 Next slide, please.

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

15 Next slide, please.

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

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

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

1 levels of radiation.

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

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

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

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

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

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

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

23                   Thank you.

24                   I will turn the microphone over to Dr. Palestro.

25                   DR. PALESTRO: Thank you.

26                   May I have the first slide, please?

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

5 Next slide, please.

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

11 Next slide, please.

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

16 Next slide, please.

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

19 Next slide, please.

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

25 Next slide, please.

26 Our first charge was to determine if the current

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

4 Next slide.

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

9 Next slide, please.

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

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

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

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

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

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

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

22 Next slide.

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

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

4 Next slide, please.

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

11 Next slide.

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

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

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



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

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

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

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

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

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

8 Next slide, please.

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

18 Next slide, please.

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

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

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

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

8 Next slide.

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

15 Next slide, please.

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

19 Thank you.

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

22 MR. MATTMULLER: Good morning.

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

1 Next slide.

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

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

20 Next slide, please.

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

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

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

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

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

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

16 Next slide, please.

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

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

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

2 (Laughter.)

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

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

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

17 Next slide, please.

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

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

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

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

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

15 Next slide, please.

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

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

1 Next slide, please.

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

6 Next slide, please.

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

10 First, the 10 microcuries. Dr. Langhorst of our  
11 Committee dug into the Law Library at Washington University and  
12 found all The Federal Register notices referenced in Appendix B.  
13 From those notices, she found the actual methodology that the NRC  
14 used when it first calculated the labeling values for radionuclides in this  
15 Appendix. By using this same methodology, she calculated a value of  
16 10 microcuries. That would, then, correspond to a 1,000-millicurie  
17 trigger limit for a DFP. We have extra confidence in her calculations in  
18 that this is the very same label quantity the NRC calculated for  
19 germanium-68 when it revised Appendix C to Part 20 in 1994.

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

26 Next slide, please.



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

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

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

20                   Thank you.

21                   DR. ALDERSON: Hello again.

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

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

3 Next slide, please.

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

9 Next slide, please.

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

16 Now we will review current communications.

17 Next slide, please.

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

22 Next slide, please.

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

26 Next slide, please.

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

4                   Next slide, please.

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

9                   Next slide, please.

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

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

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

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

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

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

10 Next slide, please.

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

20 Next slide, please.

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

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

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

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

8 We will begin questions this morning with  
9 Commissioner Ostendorff.

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

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

20 DR. ALDERSON: Sure.

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

26 So, I think what we are sensing from your presentation

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

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

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

16 DR. ALDERSON: Yes. Yes, it is.

17 COMMISSIONER OSTENDORFF: Good.

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

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

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

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

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

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

20 DR. ALDERSON: Thank you.

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

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

1 DR. ZANZONICO: Correct.

2 COMMISSIONER OSTENDORFF: Yes, okay.

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

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

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

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



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

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

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

15                   COMMISSIONER OSTENDORFF: Okay.

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

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

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

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

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

10 MS. WEIL: Again?

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

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

20 COMMISSIONER OSTENDORFF: Thank you.

21 DR. ZANZONICO: If I may just follow up?

22 COMMISSIONER OSTENDORFF: Please.  
23 Absolutely, yes.

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

1 physicians to their patients.

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

6 COMMISSIONER OSTENDORFF: Yes.

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

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

12 COMMISSIONER OSTENDORFF: Yes.

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

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

26 COMMISSIONER OSTENDORFF: Okay.

1 DR. ZANZONICO: So, that is my concern.

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

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

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

13 CHAIRMAN BURNS: Thank you, Commissioner.

14 Commissioner Baran?

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

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

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

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

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

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

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

14 DR. PALESTRO: Yes.

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

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

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

26 COMMISSIONER BARAN: Okay. But, going back

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

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

6 COMMISSIONER BARAN: Okay.

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

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

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

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

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

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

8 COMMISSIONER BARAN: Okay.

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

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

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

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

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

9 COMMISSIONER BARAN: Okay.

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

12 COMMISSIONER BARAN: Yes.

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

19 COMMISSIONER BARAN: Yes.

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

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

26 DR. PALESTRO: I think the initial development for



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

2 COMMISSIONER BARAN: Yes.

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

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

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

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

26 So, there has to be some measure of competency.

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

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

15 COMMISSIONER BARAN: Okay. Thank you.

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

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

1 approach that you could make.

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

12 COMMISSIONER BARAN: Thanks.

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

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

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

1 COMMISSIONER BARAN: Okay. Thank you.  
2 Thanks again.

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

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

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

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

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

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

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

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

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

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

23 CHAIRMAN BURNS: Okay.

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

26 CHAIRMAN BURNS: Okay.

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

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

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

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

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

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

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

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

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

3 CHAIRMAN BURNS: Okay. So, it does seem to me  
4 that, as I say, you indicated an interesting sort of developmental history  
5 here between the last revision, Part 20, in the early nineties; also, Part  
6 30 in terms of how some of the exemptions and quantities are stated.  
7 Sort of an interesting development.

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

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

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

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



1 it is the contexting that could be improved.

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

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

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

11 CHAIRMAN BURNS: Okay.

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

14 CHAIRMAN BURNS: Okay.

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

19 CHAIRMAN BURNS: Okay. Thanks.

20 Ms. Weil?

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

1 CHAIRMAN BURNS: Okay. Thank you.

2 My time is up. Commissioner Svinicki?

3 COMMISSIONER SVINICKI: Thank you all again.

4 Let me begin by expressing in the most heartfelt way that I can my  
5 gratitude for the work of the Committee, not just the members who  
6 presented at the table today. I know a number of other Committee  
7 members are here sitting in the audience.

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

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

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

1 settings.

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

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

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

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

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

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

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

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

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

1 recommendation.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

1 of imaging.

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

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

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

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



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

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

12 With that, we are adjourned.

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

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