UNITED STATES OF AMERICA

NUCLEAR REGULATORY COMMISSION

+ + + + +

MEETING WITH THE ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

+ + + + +

PUBLIC MEETING

+ + + + +

TUESDAY,

APRIL 14, 2015

+ + + + +

The Commission met in the Commissioners' Conference Room, 1st Floor, 11555 Rockville Pike, Rockville, Maryland, at 9:30 a.m., Stephen G. Burns, Chairman, presiding.

PRESENT

STEPHEN G. BURNS, Chairman

KRISTINE L. SVINICKI, Commissioner

WILLIAM C. OSTENDORFF, Commissioner

JEFF BARAN, Commissioner

ALSO PRESENT

BRUCE THOMADSEN, ACMUI Chair

FRANCIS COSTELLO, ACMUI Member

VASKEN DILSIZIAN, ACMUI Member

CHRISTOPHER PALESTRO, ACMUI Member

LAURA WEIL, ACMUI Member

MARGARET M. DOANE, OGC

ANNETTE L. VIETTI-COOK, SECY

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

9:35 a.m.

CHAIRMAN BURNS: Okay. I want to welcome our ACMUI members here today, and we're holding this meeting with the Advisory Committee on the Medical Use of Isotopes. This is an opportunity for the members of the Committee to provide their views on significant issues that have come before the Committee.

Before we begin, on behalf of the Commission I would like to take this opportunity to congratulate Dr. Bruce Thomadsen, Chairman of the Advisory Committee, on his recent honor of being presented with the Ulrich Henschke Award by the American Brachytherapy Society. I understand this is the highest honor that the Society can bestow on a practitioner in the area, and so we're very fortunate here at the NRC to have someone whose achievements are well recognized serving as the Chair of the Committee and providing guidance to the Staff.

DR. THOMADSEN: Thank you very much.

CHAIRMAN BURNS: You're welcome. You're welcome.

We're going to be briefed today by several of the Committee members on various topics.

Chairman Thomadsen will provide an overview of the Committee's work since our last meeting, and the work that remains ahead. Ms. Laura Weil will discuss Patient Rights issues before the Committee. Dr. Vasken Dilsizian will discuss the Committee's comments on the Advance Notice of Proposed Rulemaking for 10 CFR Part 20. Dr. Christopher Palestro will discuss molybdenum-99 production and impacts on the medical community. And Mr. Francis Costello will discuss the Committee's views on yttrium-90 microsphere brachytherapy, and I want to say hi to Frank who I worked with many years on the Staff when I was an attorney here, an earlier NRC career.

The presentations will be followed by a Question and Answer session with the Commission. Before I begin --- before we begin, would any of my Commissioner colleagues like to make any remarks? And is Commissioner Svinicki on the phone pending her ---

MS. VIETTI-COOK: I don't know. Commissioner Svinicki, are you still on the phone?

CHAIRMAN BURNS: No, okay. Hopefully, the traffic will clear.

So again, Chairman Thomadsen, would you please begin your presentation.

DR. THOMADSEN: Thank you very much, Mr. Chairman. It's a pleasure to be able to come and tell the Commission exactly what we've been up to, and we've been up to an awful lot lately.

The ACMUI exists to advise the NRC Staff and that way you, the Commission, on policies of medical uses of radionuclides. Also, to provide technical assistance and serve as consultants to the Commission. Next slide, please.

We have members of the Committee that represent various stakeholders in the medical radiation arena, including health care administrators, nuclear medicine physician and a physicist, two radiation oncologists, and a medical physicist, nuclear cardiologist, diagnostic radiologist, nuclear pharmacist, radiation safety officer, patient right advocate, Agreement State Representative, and a U.S. FDA representative giving a wide range of viewpoints to all of the issues that we discuss.

Some of the topics --- next slide, please. Some of the topics addressed by the ACMUI in the last six months have been refining some of the aspects of the 10 CFR Part 35 rulemaking, issues involved with patient release following iodine-131 therapy -- next slide, please --- NRC's Medical

Policy Statement, the ACMUI bylaws, inconsistencies in the tables in regulations leading to problems with decommissioning germanium-68 gallium generators --- next slide, please --- medical events for all medical applications with particular attention to those involving yttrium-90 labeled microspheres, medical event databases --- next slide, please --- the physical presence requirement for gamma stereotactic radiosurgical units, safety culture and the relationship between the Nuclear Regulatory Commission and the medical community, issues concerning the supply of molybdenum-99 and the Advance Notice of the Proposed Rulemaking for 10 CFR Part 20. Next slide.

Our current topics, what we're currently talking about in the Committee include continuing discussions of patient release, the germanium-gallium decommissioning funding plan issue, review of the medical events, compatibility categories for medical events, continuing discussions of physical presence requirements for gamma stereotactic radiosurgery units, Part 35 rulemaking status, abnormal occurrence status, radioactive seed localization guidance, patient intervention definition and guidance for handling

bodies of the deceased containing yttrium-90 microspheres. Also, the possibility of establishing a periodic stakeholder's topical meeting on an annual or biannual basis.

The present and future of the Committee is discussing a number of issues that have come up very recently, and the number seems to be increasing. Our workload is remaining quite heavy, not overwhelming, but the issues are very interesting, and the possibility that it may be increasing is very likely, particularly if we do have stakeholder meetings.

And with that, I will conclude. That's what the Committee has been doing, and is likely to be doing. And I will now turn the presentations over to Ms. Laura Weil, who is our Patient Rights Advocate.

MS. WEIL: Thank you for the opportunity to talk about some aspects of patient advocacy in the context of the ACMUI.

The welfare of patients is the central component of all ACMUI deliberations, and we are quite earnest about our professional and ethical responsibility to protect patients and patient's rights.

Members of the ACMUI are distinguished

by particular fields and expertise in medical arenas that use radiopharmaceuticals, and as the Designated Patient's Rights Advocate on the Committee, I have a dedicated responsibility to represent a constituency comprised only of patients, and I have no dual accountability to any other clinical or regulatory sphere. Next slide.

So, I would like to explore briefly three broad categories of issues that have recently been discussed and mentioned by Dr. Thomadsen. Each has a significant patient advocacy component. I'll illustrate each category with specific examples.

The broad issues include medical event and abnormal occurrence reporting, public health implications of regulatory decisions, and licensing-related access considerations. Each of these issues has an underlying common thread; the regulation's potential for unintentional creation of barriers to care limiting patient's access to needed medical treatment. Next slide, please.

The ACMUI was asked to participate in fine tuning the definitions of medical event and abnormal occurrence. The definitions of these reportable events have to be carefully crafted so that they're used as an effective tool for improving patient safety and licensee accountability.

Definitions should facilitate capture of those incidents that represent opportunities for identifying and correcting problematic issues, or processes, or individuals that cause preventable harm.

Microspheres infusions and permanent implant brachytherapy have a disproportionate number of reportable events. The challenge is to develop regulatory language where licensee failures in proficiency and due diligence can be identified without unnecessarily censoring licensees whose patients experience negative unanticipated outcomes unrelated to preventable factors.

Unclear regulatory language should not result in making clinicians shy away from offering patients useful therapy like microsphere infusions and permanent implant brachytherapy simply because each has a disproportionate incidence of unreasonably defined reportable events. Next slide, please.

The ACMUI has been asked on several occasions to comment on the Patient Release Rule of 1997. At issue has been whether or not patient release is safe. While all members of the ACMUI believe that patient release from licensee control

after administration of iodine-131 can be in the vast majority of cases a safe and cost-effective way to manage the post-treatment period. There's been much discussion, and some concern about how this is actually being managed in real practice across a wide range of treatment facilities.

When the 1997 iodine-131 Patient Release Rule was put into practice, health care insurers were given solid grounds for refusing to cover even a short hospital isolation for any patient treated with iodine-131. The public health issue is to balance the tension between two competing realities; the first being the unnecessary health care resource use in hospital stays for all patients, and the second being preserving the right to a hospital stay for those few patients who are truly unable to appropriately isolate themselves during the post-treatment period.

The repercussions of patient release range from the mundane to the truly sobering. There's ample anecdotal evidence of households that have been banned or fined by refuse carting and disposal services because iodine-131 patients in those homes were not adequately instructed regarding trash isolation after their treatment.

Their household trash sets off radiation detector alarms when it's collected, and this causes burdens for the householder, for the carting company, and for the municipality that has to investigate the radiation alarm.

This, of course, could be prevented with proper instruction prior to iodine-131 treatment. And more sobering, young children in the household of an iodine-131 patient can be exposed to radiation if the patient has not been adequately instructed about the need for isolation.

These patients are predominantly women at an age when they could have children at home, and the cause of the problem, this poor instruction problem can be complex. It can be housing-related, a single bathroom in the home for use by everyone, including the patient. Bathrooms are the most significantly contaminated room in the environment of the patient who has received iodine-131. They can be language-related. The instruction for isolation was, perhaps, not provided in a language that the patient and the family easily understand, or simply that the licensee did not provide adequate instruction about the post-treatment isolation period at all, or did not provide instruction in a way that allowed the patient time to make a

realistic plan for several days of isolation. There's ample anecdotal evidence that patients are not uniformly well informed about the realities of the post-treatment isolation period. Next slide, please.

Creating and managing regulations to promote patient safety and licensee accountability has to be balanced against compromising a patient's right to reasonable access to treatment with radiopharmaceuticals.

The ACMUI was asked to advise the NRC regarding how users of radium-223 dichloride, which is an injectable alpha emitting radiopharmaceutical, should be licensed. This was the first of potentially many injectable alpha emitters to be approved for therapeutic use.

The regulatory goal is to provide licensees with appropriate guidelines for safe administration of the drug and to allow regulators to monitor such safe use with clear and enforceable standards. The ACMUI did not want to recommend something that would create unreasonable roadblocks to patient's timely access to this highly effective palliative therapy.

The ultimate decision to recommend licensing radium-223 dichloride under 10 CFR Part

35.300 was made with the above considerations in mind. We hoped this recommendation would facilitate safe access for patients without unduly burdensome licensing requirements for clinicians.

Another recent example of ACMUI discussion involves the use of the new gallium-68 drugs for diagnostic PET imaging for neuroendocrine tumors. These new gallium-68 drugs provide many benefits to patients. They provide vastly superior diagnostic images, and require only one day versus two days to image. They have a lower radiation burden, and are less expensive compared to the spectra currently in use today.

They have been used for several years in Europe to manage --- to image this diverse class of neuroendocrine tumors, and the PET gallium-68 drugs have been granted orphan drug status by the FDA. Currently, drug sponsors and the FDA are working together to gain approval for these important diagnostic radiopharmaceuticals. However, an NRC regulation has created an almost insurmountable and likely unintentional roadblock to broad patient access to these new diagnostic isotopes.

The gallium-68 has a short half-life of 68 minutes, and is produced via a small

shoebox-sized generator from its parent isotope, germanium-68. The short half-life precludes the possibility of transporting the drug from central pharmacies for wider distribution and use.

The problem lies in the fact that currently a decommissioning funding plan is required for the use of a 50 millicurie gallium-68 generator due to the small regulatory limit of 10 millicuries. The outcome of the small regulatory limit is that licensees find themselves responsible for an extremely expensive and time-consuming decommissioning funding plan requirement, to the extent that health care institutions will be reluctant to include the gallium-68 generators in their radiopharmaceutical arsenal.

Our concern is that patients who suffer from neuroendocrine disorders, many of whom are children, will be in danger of being regulated to inferior and more physically burdensome alternative treatments all caused by a regulatory quirk that requires a decommissioning funding plan for a gallium-68 generator. Next slide, please.

In summary, it would be safe to say that any given deliberation of the ACMUI has embedded patient advocacy components. We strive to recommend balancing regulatory imperatives and patient

safety without creating unreasonable barriers to medical care.

Thank you. I'll now introduce Dr. Vasken Dilsizian.

DR. DILSIZIAN: Thank you, Laura. It's a pleasure to represent the Committee, and we were charged to make recommendations in answers to specific issues and questions that were brought to us by the NRC on the Advance Notice of Proposed Rulemaking for 10 CFR Part 20. Next slide, please.

There were six issues that were identified by the NRC, and we'll address all six of them briefly. We will be supporting three issues, one, two, and five, and will not be supporting issues three, four, and six. Next slide, please.

So briefly, issue number one is regarding updating the 10 CFR Part 20 to align with ICRP-103 methodology and terminology. The ACMUI supports replacing the terminology total effective dose equivalent with effective dose. Total effective dose equivalent is an outdated term and no longer used other than in NRC's regulatory literature. Total effective dose equivalent while similar in concept to effective dose differs largely in technical detail. It uses quality factor rather than radiation-weighting factor, and different

tabulations of the tissue-weighing factor which does not include all the tissues and organs. Next slide, please.

Issue number two relates to the occupational dose limit for events of the eye. The ACMUI supports changing the occupational dose limit of the lens of the eye from 15 rem to 5 rem. And this is based on recent human epidemiological studies which have suggested that reduced transparency of the lens of the eye may occur at significantly lower doses of radiation, ionizing radiation than previously estimated, which is termed radiation cataract. And this radiation cataract has actually distinct anatomical location which is posterior subcapsular region of the lens of the eye, which differs from age-related nuclear location of the cataract or in diabetic patients with cortical location, so we have a thumb print or a roadmap where there's a specific radiation cataract. Next slide, please.

And the personnel exposed to byproducts material include repair or maintenance of cyclotrons. From the medical perspective, those who are involved in fluoroscopic x-ray procedures, such as intervention radiologists performing yttrium-98 microsphere therapies, cardiologist performing

intravascular brachytherapy, and all the associated x-ray personnel in the room.

So, in a relatively busy interventional suite, the estimated annual dose to lens of the eye ranges from 4 to 8 rem. And, therefore, this is a reasonable range regarding regulation to request that the regulatory dose be down to 5 rem. Next slide, please.

There are three broad categories of shielding by which this can be accomplished. Number one, protective leaded eyewear glasses which can be prescriptive eyeglasses, as well; portable/moveable transparent scatter-shielding screen. And the third, which is a more expensive option but it's very effective, is wearing a personal protection whole body suit with 1 millimeter lead-equivalent acrylic face shield and apron. And all of these have been shown to effectively decrease the dose to the lens. The leaded eyewear reduces the lens dose by a factor of 5 to 10. The scatter-shield screen will reduce the lens dose by a factor of 5 to 25, and if you use both together it will reduce the dose by 25-folds or higher.

What are the implications of the change from 15 rem to 5 rem? Well, this will certainly

require changes in the fluoroscopic x-ray safety programs making the use of personal leaded glasses or eye protective shield, we recommend it to be mandatory for those physicians and trainees who are practicing exactly at the table with the patient. And, of course, the ancillary staff, as long as they're about 3-feet away from the fluoroscopic table, it's been shown that the radiation exposure will be 10-fold reduced to those ancillary staff. And, therefore, we would recommend that those ancillary staff be wearing eye shield, but it's not mandatory.

Now, of course, if there is any procedure that has significant non-uniformity in the radiation field in terms of body versus the eye, those personnel may need to utilize eye-specific dosimeters which can be worn directly above the eyebrows with a head strap.

Issue number three, that relates to limiting the dose of the embryo and fetus of a declared pregnant occupational worker. The ACMUI does not support reducing the dose to the embryo, fetus, or declared pregnant woman from 5 millisieverts to 1 millisievert, or 500 millirem to 100 millirem.

Unlike the data that I presented to you

regarding to the dose to lens of the eye where there's plenty of scientific epidemiological data, the risk of cancer from in utero radiation exposure is a controversial subject. While the dose limit to the embryo or fetus should certainly be kept as low as reasonable, we all agree with that, there is no scientific data, however, that there's increased risk in declared pregnant occupational women with the current 500 millirem dose limit. Next slide, please.

The ACMUI does not know of a source of data other than that gathered by the vendors providing individual monitoring devices. And based on our collaborative knowledge, deep effective dose equivalent measurements from individual monitoring devices assigned to these declared pregnant women remain well below 500 millirem over the gestational period, and the latest NCRP report continues to recommend dose limit of 50 rem per gestation month, which would be similar to the recommended dose of 500 millirem per year.

Now, I would like to add at this point that the additional potential recommendation on changing the regulatory dose to 100 millirem would be that it is equivalent to the variability of the background radiation dose that is currently present

across the United States among the states. So, if we're going to have a regulatory rule, it will be tough to control that and maintain that because it would be difficult to differentiate the incremental dose of 100 millirem in a pregnant woman beyond that is already variable with the background dose. That would be extremely difficult to regulate.

So, based on these findings, the other potential --- next slide. The other potential negative impacts of lowering the dose limit would be that a more restrictive limit could result in an increase in individuals choosing not to declare their pregnancy, particularly in the early gestational period in order to insure their continued employment.

The other potential possibility would be that there would be non-compliance of wearing proper dosimetry in order to keep their occupational dose within the lower limit to maintain their employment. And this, of course, would result in an inappropriate bias in potentially selecting female applicants for these ionizing radiation-dependent jobs.

Issue number four relates to individual protection, ALARA planning. The ACMUI does not support having specific ALARA planning and

implementation requirements to 10 CFR Part 20 regulations. The current Part 20 requires ALARA programs, but does not provide specific ALARA planning and implementation requirements, and so allowed licensees to design the ALARA requirement that are most appropriate for their own activities.

The medical users of radioactive materials rarely experience situations where workers' doses approach regulatory limits. Many of them already utilize administrative control levels to maintain doses as low as possible.

The risks --- next slide, please. The risk and safety cultures of different industries and different licensees within the same industry differ so much that providing the same compliance-based requirements on all licensees will not be effective. And, moreover, defining what may be reasonably achievable is an inherently subjective process. So, the best methodology would be to maintain the status quo and not impose any further prescriptive requirements. Next slide, please.

Issue number five relates to metrication, units of radiation exposure and dose. The ACMUI does support the change to use international system of units in radiation

protection regulations. The use of both international and traditional units should be used consistently throughout the regulation with the emphasis on the international unit first as a regulatory standard followed by the conventional unit in parenthesis. This should be done as a means to effect a transition to the sole use of international units in the future. This should not cause undue burden or hardship upon any licensee or class of licensees as all nations other than the United States have already accomplished this transition to the international units. Next slide, please.

Issue number six relates to reporting of occupational exposure. The ACMUI does not support expanding additional categories of licensees that should be required to submit annual occupational exposure reports under 10 CFR 20.2206(a).

The ACMUI does not believe that the NRC should act as the nation's repository for occupational radiation exposure data, particularly since NRC does not have regulatory authority over all ionizing radiation sources. It also does not make sense to collect national data for only one area of occupational radiation exposure considering that the more extensive exposure is from

x-rays. Next slide, please.

Occupational doses have low averages for medical use licensees and licensees which support them. Accordingly, many of these workers are not even assigned personal dosimetry; thus, requiring national occupational dose tracking of those radiation workers who do require individualized monitoring would lead to unrealistically high estimates of average occupational dose for medical licensees. In essence, the data would be unintentionally biased towards higher doses since most of the low-dose individuals will not be even monitoring with personal dosimetry.

Moreover, occupational dose does not include doses received from background radiation, medical administration of diagnostic of therapeutic doses in these individuals, or some voluntary participation in medical research programs which will not be captured in the dosimetry. Next slide, please.

And NRC does not, of course, regulate all use of radioactive materials. Most are regulated by Agreement States. If the purpose of a central database is to assess total annual occupational exposure for radiation workers, the NRC's limited

regulatory authority would not make an ideal federal entity to manage such a central database. Next slide.

So, in conclusion, the ACMUI recommends NRC use a similar implementation plan that was used for the latest significant change of 10 CFR Part 20, 1991 where the licensee could choose to implement the regulatory change any time within a given time frame, and the ACMUI recommends a time frame of at least three years to allow implementation of procedure, training, hardware, and software changes needed to comply with the new regulatory requirements.

Thank you very much for your attention, and I would like to present Dr. Palestro to present his topic on molybdenum-99.

DR. PALESTRO: Thank you. In the next few minutes, I'm going to address molybdenum-99 production and its impact on the medical community. Can I have the next slide, please?

Molybdenum-99 is the parent of technetium-99m, and technetium-99m is the modern nuclear medicine imaging workhorse. Worldwide, technetium-99m is used in approximately 80 percent of the 30 million diagnostic nuclear medicine procedures that are performed annually. And

technetium-99m studies in the United States, approximately 50,000 of these are performed on a daily basis. Next slide, please.

North America, nearly 50 percent of the 30 million procedures using technetium-99m annually are performed. In Europe, approximately 20 to 23 percent of these procedures are performed, and Asia and the Pacific regions account for another 20 to 27 percent. It is estimated that technetium-99m nuclear medicine procedures worldwide will increase by about 1 to 2 percent annually through 2020. Next slide, please.

The European Union produces approximately 45 percent of the world's molybdenum-99, and consumes about 22 percent of the molybdenum-99. Canada produces about 40 percent of the world's molybdenum-99, and uses about 4 percent of the total world production. The United States, which produces no molybdenum-99, consumes nearly 50 percent of the world's molybdenum-99. Next slide, please.

Now, in getting from molybdenum to 99mTc and its use in nuclear medicine and for patients, there's a supply chain. It has several different components. The first component is a nuclear reactor. We have neutron bombardment of uranium

target produces daughter isotopes which include molybdenum-99. Then the second component is isotope production which consists of both the extraction and purification of molybdenum-99. Third is the manufacture of the molybdenum-99 technetium-99m generator, and fourth is the distribution of these generators. And each of these components typically are organized and controlled by different organizations, different corporations. Finally, the distribution of these generators goes in some cases to hospitals, but in the United States primarily to radiopharmacies. Next slide, please.

It's important for us to be cognizant of the fact that the molybdenum-technetium supply chain is fragile, and there are several reasons why it is fragile. Number one, the entire worldwide production of molybdenum-99 takes place at fewer than 10 sites, none of which are in the United States. So, the impact of any one of these sites, particularly the larger ones, going down for a protracted period of time can be quite significant, as we learned a few years ago.

Complicating matters is the fact that many of these reactors, including several that I've listed here, the NRU in Canada, the HFR, the Osiris BR2 in Europe, and Safari in South Africa, which

account for about 95 percent of the total world's production of molybdenum-99 are more than 45 years old. Several of these reactors are scheduled or have been scheduled for decommissioning over the next several years. And, admittedly, while the decommissioning dates have continued to be postponed, and likely will continue to be postponed for the foreseeable future, their age alone is cause for concern. They can have extensive down time, as we learned in 2008 to 2010 when the NRU in Canada, and the HFR in the Netherlands, which together account for nearly 70 percent of the world's molybdenum-99 production, were out of service for 15 and 13 months respectively.

Finally, the United States produces more than 90 percent of the world's highly enriched uranium. And the U.S. has decided for security reasons at some point in the not too distant future to stop exporting highly enriched uranium. Next slide, please.

What are the consequences of interrupting the molybdenum-technetium-99m supply chain? Well, we had a chance to experience that and come to understand some of these problems during those interruptions of 2008 to 2010. And, ultimately, it potentially can and did wreak havoc

on patient care.

For example, some of the effects on diagnostic testing include postponed or cancelled studies, the use of alternative less desirable radiopharmaceuticals, the use of alternative more expensive and not necessarily more accurate procedures. The effects on patient care? Well, there were delays in diagnosis, delays in treatment, and in the United States alone from 2008 to 2012, there was nearly a 10 percent decrease in the number of nuclear medicine studies performed. Next slide, please.

So, how did we cope, or how can we cope with the molybdenum-technetium supply chain interruptions? Well, what we developed, what we learned for that period of 2008 to 2010 was that the solutions were really short term, or perhaps better described as stopgap. One solution is certainly to more frequently elute the generator. The technetium activity is there, elute it, remove it from the generator, use it. That works provided you have a generator, but if the generator is not available, you can't elute it. Revised examination schedules, increasing the work day so it could elute the generator more frequently, scheduling cases on Saturdays and sometimes Sundays because the

technetium is available at that time, make use of it. It certainly provides greater access to the patients in most need. And we also grouped studies together, like studies. Instead of doing a bone scan today, and a bone scan tomorrow, consolidate them all, or try to, on one day.

Well, that works to some extent, but it also results in canceled studies. When studies need to be performed immediately, the referring service feels that they can't wait, they go to seek alternative studies. Next slide, please.

Another option for coping with these interruptions, decrease the amount of administered activity. Give less radioactivity to each patient so that we can image more patients. And, you know, on the surface that sounds quite good, and certainly is viable. The downside is that it requires a longer imaging time to have a satisfactory or comparable image quality. And, unfortunately, the vast majority of the patients that we image are ill. They're often in pain making it difficult for them to lie still for longer time periods.

In the case of the children, what is a 20-minute scan turns into a 30-minute scan or a 35-minute scan. And for the 20-minute scan perhaps they could lie still, for the 35-minute scan maybe

now we have to go to sedation. So, there are significant ramifications to decreasing administered activity.

What about alternative radiopharmaceuticals? Nuclear cardiology accounts for about 60 percent of all technetium-based studies, and during the interruptions of 2008 to 2010, it wasn't uncommon to switch from technetium-based agents back to thallium-201, which is really a throwback. Thallium-201 offers inferior image quality, increased patient radiation exposure, and in some cases an increased downstream testing and increased cost. Next slide, please.

There are other radiopharmaceuticals for nuclear cardiology, nitrogen-13, rubidium-82, positron emitters, excellent radiopharmaceuticals, but here we were confronted with a relatively limited number of PET imaging systems versus the conventional gamma camera SPECT imaging systems. Bone scintigraphy accounts for about 20 percent of technetium-based studies, and there certainly is an excellent alternative to the bone scan, fluorine-18. Unfortunately, again, fluorine-18 is a positron emitter so we are limited --- have to deal with limited availability. And

further complicating matters is fluorine-18 is not yet reimbursable. Next slide, please.

So, while these measures certainly enabled us to get by in the short run, they're not long term solutions. What, in fact, then is needed? Well, what is needed is a readily available consistent supply of molybdenum-99m so that we'll --- molybdenum-99 so the technetium-99m will be available to facilitate the performance of nuclear medicine procedures that are necessary for patient care. Next slide, please.

Long-term solutions, what are they? Well, certainly, one long-term solution would be to decentralize molybdenum-99 production. As I said previously, the entire worldwide production is accomplished at fewer than 10 sites. If there were 15 sites, if there 20 or 25 sites, then the impact of one, or two, or three sites going down at any given time would be of far less magnitude than what we experienced in 2008 to 2010. For a lot of reasons, that's probably not likely to happen.

I think a more realistic and probably a better solution, certainly for the United States, is to develop a reliable domestic supply of molybdenum-99. At least under these circumstances we will be in control of our own destiny. Next slide,

please.

At the moment, there are two companies that are seeking or in the process, I should say, of developing molybdenum-99. One is NorthStar Medical Technologies which makes use of a neutron capture technology. They had planned to be operational in 2015, although, it looks like 2016 is probably a better estimate of when they might be operational. Initially, they would anticipate being able to provide about 5 percent of the United States molybdenum-99 needs. When they are fully operational at some time in the future they expect to supply about 50 percent of our country's needs.

Shine Medical Technologies is the other company. They make use of a low enriched uranium technology, and they say that when they are fully operational they will be able to supply perhaps as much as one-third of the world's molybdenum-99 needs. They originally had hoped to be operational by the end of 2017, but now it appears that they're not likely to be operational until sometime in about mid-2018.

So, in summary, we have made some strides towards coping with interruptions in the molybdenum-99 supply, but we still have a way to go. Thank you, and now I'll turn the session over

to Mr. Francis Costello.

MR. COSTELLO: Thank you. As Chairman Burns mentioned, both he and I had a previous NRC career, and mine was for 30-1/2 years, and during that time I never had the opportunity to brief the Commission, so I'm very honored to be able to be here today.

About a year ago, you know, I work in Pennsylvania, we had an event involving microspheres where they were shunting to the GI tract. And we'd never seen one of those events before, so I did a little literature research and looked in EDMED and another Agreement State, Ohio, had a couple of events like that. And then I looked further in the literature, which indicate that actually this was a recognized risk of the treatment, and might be expected to happen a couple of percent of the time.

So, I talked to some of the RSOs at our larger institutions, mostly in Philadelphia, and they indicated that it may very well be that this was -- it may be that many of the uses were not consider to be medical event then -- if they did everything right themselves. And despite that, the spheres went to the GI tract. So, having just been appointed to the ACMUI, I brought it up at the ACMUI

spring meeting, and they set up a subcommittee to look into this. So, I'm reporting back to you today as to what the subcommittee did, and make a few comments on what the implications are. Next slide, please.

A little bit about the treatment itself. For the most part, these treatments are done as a palliative treatment. There's some evidence it can improve survival, and it perhaps in fortunate cases it could enable the patient to become ready for a transplant. But mostly, this is done as a palliative treatment. Next slide, please.

The procedure, and there's an image I'll show you in a second, the microspheres go through a catheter, go to the hepatic artery, the branches, and the microspheres themselves are too large to pass through the capillaries and become permanently implanted in the tumor, and they then irradiate the tumor with a therapeutic dose. Next slide, please.

You can see an image of this there, and if you note, in a couple of places there is blockages, and those are there to prevent the microspheres from going to places they shouldn't go; prevent them to be shunting to the lung, and prevent shunting to the GI tract. So, there's mapping that's done in advance of the treatment to

make --- to do the very best they can to make sure that these spheres only go to the liver and don't go to the GI, or go to the lung. Next slide, please.

So, each patient must meet strict selection criteria. And each procedure is meticulously individualized for the patient to make sure that the right dose is given, of course, and to make sure that the spheres will not go to places they shouldn't go. And the idea is to eliminate or minimize the known risk of activity deposit, non-target tissues, particularly into the lung, and into the GI tract, which is what we had in Pennsylvania, and it also happened in Ohio. Next slide, please.

So, a subcommittee was formed at the spring ACMUI meeting to determine well, what conditions should be a reportable medical event, because it was apparent that there are practitioners who are doing this, and because they put the spheres exactly where they wanted them to go and they blocked the vessels off the best they could, may not have been reporting these because the procedure had gone well despite that the spheres wound up, perhaps, in the GI tract. So, the Committee was looking into well, what can do about that? What's the right thing, and what's the right thing for the guidance to be

done? As I'm sure you know, this treatment is done under 35.1000, so most of the requirements are found in the guidance which is on the website which has been changed quite a few times since the first time this was placed under 35.1000. Next slide, please.

So, our charge was recommendations for relevant changes to the guidance. And the guidance, most recent guidance was in 2012. next slide, please.

However, we were also given an expanded charge at the discretion of the subcommittee, we could determine whether additional medical event issues related to --- unrelated to GI deposition also require considerations. And we were to offer specific recommendations to the Staff on related regulatory guide changes. Next slide, please.

So, the Committee met on this over several months over the summer of 2014, and we voted unanimously that the current guidance needs to be modified in order to align with the new characteristics of Y-90 microsphere brachytherapy. The advances and improvements that have occurred over time to basically decrease the likelihood of these spheres winding in non-target areas. And, actually, to reflect the current medical practice of authorized users and medical teams across the

country. Next slide, please.

The conclusion was, basically, that the most appropriate metric for regulatory purposes is what was the prescribed activity in the directive, and what was the actual activity infused into the patient? The medical event report criteria should be based on a readily determined difference between the prescribed activity in a written directive and the actual activity put into the patient. Next slide, please.

You may recall, there's some similarity here between what we did in permanent brachytherapy, the same issue came up there. Specification of an acceptable GI tract and lung dose in the written directive should not be required because, basically, the goal here is that there not be shunting. Not that we're trying to set an acceptable level of shunting, but with proper mapping and proper blocking of vessels, that there will not be shunting, or significant shunting to the GI tract, or to the lung. So, the total treatment activity to be administered should require compliance measures for organs and tissues other than the treatment site.

A written --- a medical event in this case would be if there's a difference between the

actual infused activity and the activity written in the written directive. That would be the goal; except, there are some cases where stasis occurs, and it's not possible to safely infuse any more activity, and that then simply becomes a new prescribed activity. Except in the case of stasis, you compare the prescribed activity to the infused activity, and if it differs by more than 20 percent, that would be a medical event.

We recommended that the Staff incorporate these considerations into the guidance, and that they share this with the Agreement States and the licensees so they can implement it. Last fall, at the fall meeting, we provided the recommendations to the Staff, and Staff currently has them under consideration. I expect we'll be hearing from them at our next meeting.

A few points I would like to make about this. As I mentioned before, this modality is regulated under 35.1000, which gives us the flexibility of essentially changing the requirement without a rule change. I would also point out that the --- it shows how operational experience coming from Agreement States, Ohio and Pennsylvania, can be of great benefit to the NRC, to the Staff. You know, most of the licensees, those

medical licensees now are regulated by Agreement States, and getting that operational experience to the NRC is of great value to them.

In addition, the ACMUI's advice to the Staff on an issue like this is a frequent and integral part of the process for developing guidance, and it provides yet another example of the value-added by the ACMUI. Thank you.

CHAIRMAN BURNS: Thank you, Mr. Costello. And with that, I think that's it, and we'll begin with Commissioners question. Commissioner Ostendorff.

COMMISSIONER OSTENDORFF: Thank you, Chairman, and thank you all for being here. Congratulations.

DR. THOMADSEN: Thank you.

COMMISSIONER OSTENDORFF: And I just think --- I've been here --- I guess I'm the second-longest serving Commissioner after Commissioner Svinicki, but I know that after five years of being at these meetings, I continue to be amazed at what I learn and just the highlights of value that you provide to the NRC when it comes to the intersection between what we regulate and how medicine is practiced in this country, so I'm just very grateful for what all of you do.

Dr. Thomadsen, let me start off with you, please. On your Slide 7 you talk about some of the topics in your overview, and I found that very helpful. But could you just comment maybe in a little more detail, the bullet on the relationship between the NRC and the medical community? Are there any particular concerns there, or any high-level points you'd like to make?

DR. THOMADSEN: Yes. We've talked about that at a previous Commissioner's briefing, that the relation between the Commission's Staff and the facilities is very critical to try to improve the safety at those facilities. The punitive effect of some of the inspections and the way that the inspectors may characterize problems that are found can itself provide a chilling effect on the reporting of problems from a facility. And sometimes this may be intentional, and sometimes it may not. It may be that the facility may understand some things about problems they have, but they just don't want to share for fear that they may be punished in some way.

So, the safety culture that the NRC suggests for facilities to try to be open and non-punitive also could be beneficial to apply for the NRC working with the facilities, the goal being

to improve safety, not necessarily to punish those who have accidents and commit errors.

COMMISSIONER OSTENDORFF: In your communications between the Committee and the NRC Staff, does our Staff have the benefit of the knowledge of some of these specific examples where you believe there's been a chilling effect, or a punitive approach from the eyes of the inspected facility?

DR. THOMADSEN: At the briefing last time, I did use an example that was presented by an NRC Staff person at the Health Physics Society meeting last year, not this --- the one that was in Madison, where the inspect --- or the person reporting on the inspection was talking about the chilling effect at the institution of the workers who did not want to report things that would make their facility look bad, and made the assumption that that was due to the managerial policy; although, that was not clear in the presentation. What was clear in the presentation was that the NRC's Staff during the inspection and the report was definitely making statements about the facility that possibly could exacerbate any chilling effect that there might be at the facility.

COMMISSIONER OSTENDORFF: Okay, thank

you.

DR. THOMADSEN: You're welcome.

COMMISSIONER OSTENDORFF: I'm going to shift now to Mr. Costello, but I'm kind of looking at the very last slide you have, and the last bullet about, you know, the example, the benefit of ACMUI's input into the Staff. I thought that was really an effective summary of your presentation.

I guess one thing that I wanted to ask you about, but others may have an opinion here to --- and you'll have a chance to provide that. You know, as a regulatory body we, obviously, deal with rulemaking under the Administrative Procedures Act. There's a very somewhat bureaucratic process we go through to look at regulatory issues, and even with respect to promulgation of guidance. And I was just trying to think about the yttrium-90 microsphere piece and the notion of palliative care is why that's being administered in many of the cases of treatment. And do you feel like our system is sufficiently responsive time-wise to incorporate this type of feedback, and to change the guidance, or do you have any perspective on that having worked at the NRC, and being in your current position? I worry about, you know, because medicine --- I know the practice of medicine, this as a lay person,

changes every day. And practices, it's a very dynamic environment, and so --- but we're not necessarily set up to be as dynamic as the practice of medicine is. Do you want to comment on that?

MR. COSTELLO: Absolutely, sir. Modalities are covered by 35.1000, enables the NRC to be fairly nimble in changing it as they become more knowledgeable what's going on out there in the community. And this is a very good example here. I mean, the Staff can change the guidance in the website fairly easily, and I think you'll find all the Agreement States pretty much follow what's on the websites.

Changes, however, that require regulatory changes. We talked about the germanium-gallium generator, for example, changes that would seem very simple can take an inordinate amount of time because the rulemaking process is what it is. So, I'll say that the -- with regard to things in 35.1000, I think the NRC should be proud how quickly it can change the guidance and improve things. With regard to things that are in black letter regulation, it's much slower, much more difficult.

COMMISSIONER OSTENDORFF: Do you see --- you know, from your experience over your career,

do you have any suggestions on how we might be able to be a bit more responsive in this area? Again, noting that this is the practice of medicine, as opposed to perhaps some other topical areas we regulate?

DR. THOMADSEN: Yes. There's a downside of 35.1000, and the downside, it doesn't have the public comment, the public input that you have for regulations. There's a reason why rulemaking takes as long as it does, because more opportunity for the public to get involved in the process, and I understand that.

In addition, things under 35.1000 are supposedly there temporarily. And the goal of 35.1000 was to --- for new modalities until the Agency gets experience to regulate them that way, that perhaps later are incorporated in the regulations.

In all honesty, I have never understood why the simplest rulemaking takes as long as it does. You will know way better than I do. I imagine you must be as frustrated as many people are that the simplest rulemaking can take years.

My only advice would be if there's some way to, you know, make things go through the direct rulemaking process more simply for things that are

non-controversial. Again, the example of the germanium decommissioning requirements, changing them, there would be no --- no one would complain. It's an obvious change that one would want to make, if you knew the situation. But when one talks about it, it talks well, this could take years. It is incomprehensible to the outside. States are slow, but not that slow.

COMMISSIONER OSTENDORFF: Okay. I'm going to allow our Patient Rights Advocate. Perhaps, I think you maybe wanted to say something, Laura?

MS. WEIL: I just --- I think Mr. Costello has said it well. The time lag to be able to make changes that would benefit patients and clinicians, it's just such an unwieldy process. And there must be something that can be done to give relief in those situations where there's clearly a need, and no downside.

MR. COSTELLO: Can I make one more comment on that?

COMMISSIONER OSTENDORFF: Yes.

MR. COSTELLO: In 2005, the Commission which did not include anyone here, recommended that the requirements for permanent brachytherapy change from a dose-based rule to an activity-based rule. This is in 2005. It is now 2015, and the current

requirement for permanent brachytherapy is a dose-based rule. And the Chairman and I discussed this over breakfast this morning, the U.S. Constitution was written faster than that. Thank you.

COMMISSIONER OSTENDORFF: Thank you for that helpful example. Thank you all.

CHAIRMAN BURNS: Commissioner Baran.

COMMISSIONER BARAN: Well, thanks for being here, and to all of you for your service on the Advisory Committee.

Just to follow-up on the yttrium-90 microsphere issue. I wanted to get a better sense of how common is it that non-targeted organs are affected, and how avoidable is that? Is it something that's just unavoidable in certain cases, or are there practices that can improve the issue?

MR. COSTELLO: The medical practice has learned a lot over the last seven or eight years, in terms of doing the mapping in advance to prevent these spheres from going to the lung, or going to the GI tract. This is a very personalized treatment, but sometimes the body can resist what you're trying to do. And it could create new pathways after you've blocked the previous pathways.

I don't think we know how common it is.

It is rarely reported, which is the first thing that called it to my attention. It happened in Pennsylvania, it happened in Ohio, looked at the literature and you look at the package insert on this and it indicates this is an expected, you know, risk of this procedure. And it's hardly ever reported, I think because the practitioners who when they do everything properly to the best of their knowledge, don't see this as a medical event.

I really do not know how often this happens. I know that it's rarely reported in Pennsylvania. In the eight years we've been an Agreement State, I think it happened once, but I think some states have never had it reported. But you read the literature, it should happen a certain number of times.

DR. DILSIZIAN: Could I add to that?

COMMISSIONER BARAN: Please.

DR. DILSIZIAN: We do a lot of yttrium-90 therapies at the University of Maryland, and the two areas is the gastric reflux, which the physician should be able to coil the artery so that they avoid the reflux. And it's rare, it's very rare for us. We do several of these a week, and we're one of the largest centers that do these therapies.

Regarding the shunt, the lung shunt that

we're talking about, it can't be prevented by coiling the arteries. The shunt itself is a physiological shunt. The tumor itself has AV malformation so you give the microspheres, it just goes to the lung, and we can understand that before the therapy by giving MAAs and you calculate what the percent shunt is to the lung. And, accordingly, you give lower dose to prevent subsequent radiation-induced pulmonary fibrosis, if you will. And so the two --- I don't want to mix those two up.

The gastric reflux is something that you can prevent by coiling. The lung shunt is a physiological shunt induced by the tumor, which you can assess ahead of time, and then change your dosimetry accordingly. Does that help?

COMMISSIONER BARAN: That does help. And just so that I have a better understanding of this, so tie that a little bit to the guidance and what that looks like now. So, walk us through a little bit what's the essential concern with the current guidance? Is it unclear, or is it implementation too difficult, or is there another issue there?

MR. COSTELLO: I think they think that it's clear but it's not good.

COMMISSIONER BARAN: Okay.

MR. COSTELLO: The guidance would ask you to estimate the dose to the GI tract. And, basically, the medical team is trying to prevent any dose to the GI tract. It's not a matter of what's acceptable. The idea is to have none. And as you indicate, as far as the lung goes, I believe there's some situations where via the mapping, if they think the dose to the lung is too high, they reduce the dose along to the treatment. Okay? I think I've answered the question.

COMMISSIONER BARAN: Okay. Did you want to add anything, Dr. Dilsizian?

DR. DILSIZIAN: No, that's fine.

COMMISSIONER BARAN: Okay. And I take it most of you were on the Subcommittee that looked at this issue. Ms. Weil, were you on the Subcommittee, also, or no? Do you have a view on this?

MS. WEIL: Well, I think, you know, from a patient's perspective, I think the problem is, is that this is a therapy which is not I would say common, but it is of great value, and is a last resort to folks who have these intractable tumors, and who perhaps need to just survive while they're on the transplant list to get something curative. But institutions become less and less willing to provide

this particular therapy because they get reported, because there is a high incidence of reportable events associated with microsphere infusions. And that's --- you know, it creates something that is not beneficial to patients when the reportable events impede treatment in a way that isn't related to protecting patients, because it should be patient protection, it should be to identify preventable problems, and that's kind of not how it's playing out.

COMMISSIONER BARAN: So, let me ask you this, and this is for anyone who wants to weigh into this. I mean, what's your sense of whether there would be any controversial about changing the guidance in this way? Is this something that there are folks who are going to be really concerned about this, or is this one of those cases where there's going to be kind of universal agreement that this is a good idea?

DR. THOMADSEN: I'll take a stab at that one.

COMMISSIONER BARAN: Okay.

DR. THOMADSEN: And I don't think so. I think this is --- this would be a change that would not be controversial, and particularly the people who do the procedure understand that this is a

problem with physiology. It's not a problem with what they do, and so they would be in favor of it. The Patient Advocate, as you've just heard, would not want to see this limit the number of places that could do this just because of fear of having to report an event. The number of occasions in which this is a --- has detriment to the patient is few. There are some, and it is a known toxicity of the procedure. Being a known toxicity and one that is just part of having the procedure done, there seems little reason to call that an event.

COMMISSIONER BARAN: Talking more about a side effect.

DR. THOMADSEN: Yes.

COMMISSIONER BARAN: A known side effect.

DR. THOMADSEN: Yes. I'm sorry. The terminology that most lay people would have would be side effect.

COMMISSIONER BARAN: Which I ---

DR. THOMADSEN: Right, we use toxicity. Sorry.

COMMISSIONER BARAN: Right. No, that's fine. Anything else on that topic before we turn to someone else? Yes?

DR. PALESTRO: Yes. We do a fair number

of these procedures, approximately 100 per year, and I would just echo Dr. Thomadsen's comments about a lack of opposition to changing the guidance.

One of the big issues is there's no reliable way to accurately determine the dose to the gastrointestinal tract given current techniques that we have. And while I can't quote you the frequency with which these side effects occur, I think there's ample documentation in the literature, and certainly our own personal experience that the more of these that are done, the more experience that one has, the fewer --- the lower the frequency of these sorts of events.

We had one or two cases early on, and have not had any cases of GI toxicity over the past couple of years. So at our institution, at least, it would be well under 1 percent.

COMMISSIONER BARAN: Okay, thank you.

MR. COSTELLO: Just one thing.

COMMISSIONER BARAN: Yes.

MR. COSTELLO: The one thing I would remind you, of course, is we have not heard back from the Staff yet. These are recommendations that we gave the Staff at the fall meeting, and I'm hoping to hear the Staff's response to this at next fall's meeting.

COMMISSIONER BARAN: Okay. Maybe we could turn to the proposed changes to Part 20 for just a minute, or for the last couple of minutes of my time. Thank you for your comments on that.

Can you talk a little bit more about how the Advisory Committee weighed the pros and cons of the proposed change to the occupational dose limit for the lens of the eye from 15 rem to 5 rem?

DR. DILSIZIAN: Yes. Thanks. The two major areas is that there was significant epidemiological scientific data to suggest that radiation does induce cataract, number one. And that there was a fingerprint area of the lens of the eye posterior subcapsular which was related to that.

The next thing we did is to say okay, now that we do know. Now, unlike other aspects of radiation, fortunately, cataracts are easily replaceable with another lens surgically. Obviously, we need to work on the prevention rather than the therapy aspect of it.

The next was the data on what is a busy interventional laboratory, what was the annual exposure in those individuals? And I provided the data, it was before 4 and 8 rem. So, that's assuming that we're not doing all these protective measures. Now, I would admit that most radiologists and

cardiologists are wearing lead eyeglasses, but I'm not sure --- I don't think that they're wearing lead eyeglasses plus the shield, so you can actually reduce by 25-folds if you do the two combinations. So, given that the range was within that 5 rem, it wasn't too far away, we felt that it would be important for us to not just recommend but mandate prevention for cataract at these folks who are at the table, and make it a recommendation for those who are in the room, but 3-feet away from the table.

COMMISSIONER BARAN: And it sounds like the steps you take there are actually pretty straightforward, if it's just kind of the glasses and stand behind a screen.

DR. DILSIZIAN: Yes. And, again, some of these are already in place in that sense. The shield in the CAT lab, it's there. The glasses some people use. It's just that it's not used —-it would be nicer to make the recommendation more firm rather than voluntarily, if you will.

COMMISSIONER BARAN: Okay, thank you. Thanks, again.

CHAIRMAN BURNS: Thank you all, again, for your presentations. Good to get the briefings on the various aspects of the work of the Committee.

One question I have, maybe start going

back to this area that Mr. Costello and Ms. Weil were talking about, and anyone can sort of respond to this. But, I mean, I remember --- I mean, I started to work here at the time when we called these medical events misadministrations. And I forget and, Frank, you'll have to remind me when that rule change, I think that may have been in the '90s. And I understand, and I appreciate that, but --- and this is maybe in part --- it's not really a rhetorical question, but the question, what's the effect --- and maybe those from the medical --- what's the effect of identifying something as a reportable event? And when I started saying is not from the standpoint of the NRC, because I think I understand from the NRC, but under --- I think behind your comments there's a question of there's an impact of labeling something as a reportable event. So, I'd appreciate actually anyone's comments or reflections on that.

MS. WEIL: I think even a little further upstream what's the purpose of collecting this data? And the purpose of the collection should be to improve patient safety, to improve clinical outcomes, but that's not how it works out, necessarily, because the definitions of these reportable events does not --- it doesn't

necessarily relate to something that can be corrected. And it's those two pots that we have to reconcile, the preventable stuff, and the unpreventable stuff.

Certainly, reporting preventable stuff and fixing the procedures and the processes, the institutional processes that lead to them would be a wonderful outcome, but the unpreventable stuff is different, and those need to be teased apart.

CHAIRMAN BURNS: Yes, Frank?

MR. COSTELLO: I can't tell you how many times in speaking to licensees either individually or sometimes as a group, I will say medical events are not violations. I mean, sometimes we follow-up on a medical event, it's a clear inspection. And we actually will praise the licensee for having identified and take corrective actions for this medical event. However, I recognize that --- and they will tell me that sometimes they think that I'm naive; that these things are public, that their management is unhappy, patients may hear about it. You may recall the fellow at the VA a number of years ago, and they'll tell me stories of other inspectors or other regulatory agencies other than Pennsylvania coming down very hard on licensees for having reported a medical event even though they

may have done everything right.

It's up to us, speaking now as a regulator, it's up to us to treat these things as they're supposed to be treated; that the simple reporting of them is something as a licensee is a good thing. They identified it, and reported it, and took corrective actions. There may be times where the causes of something is another story, but yes, I think there are licensees who when told that a medical event is not a violation think that the person telling them that is naive. They don't understand the real environment that these people work in.

CHAIRMAN BURNS: Okay. Anyone else? Dr. Dilsizian, I've got a couple of questions on the proposed Part 20. Actually, I saw the one recommendation with respect to the conversion to international units sort of somewhat bemused because I just came from OECD Nuclear Energy Agency and my colleagues in radiation protection were very amused at the Americans and their practices. I said well, I'm here now. I said I'm here for legal advice, not for whatever, but anyway, so it's interesting.

Is there perhaps --- is there a resistance, perhaps, other than it's always difficult, you know, making --- you know,

relabeling things or something like that. Where do you see the potential resistance to that recommendation?

DR. DILSIZIAN: I suspect it won't —-there won't be a lot of resistance. It's just, you know, it's human nature. You're used to certain terminologies, you're resistant of change. But I guess in our investigation we found out that a lot of the --- even in the United States, a lot of these treating doses have already switched to international doses.

CHAIRMAN BURNS: Okay.

DR. DILSIZIAN: So, there is already a large adaptation when it comes to exporting and importing. And all that we need to do now is within the United States kind of move that into that direction.

I just think that it's just a matter of a few years, a period of time just getting used to the reporting both, and at some point to just give up.

CHAIRMAN BURNS: Okay. As I say, I was constantly sort of poked by colleagues at NEA over this issue. One other thing to make sure I understand the question on ALARA, or ALARA programs. I take it, and I haven't looked at the particular

recommendations, ANPR, in particular. But I take it the concern is that the description that would be --- there are more precise guidelines or criteria for particular ALARA programs. Is it that the nature of it?

DR. DILSIZIAN: Yes, because there's such different applications with this equipment, machinery versus medical use, to have one prescription which is relatively subjective to kind of guide all of them would be difficult. And I also understand that the ones that we would be concerned with that would approach the ALARA limit, the large machines are actually under Agreement States more than under NRC's, so it seems like we're not --- we don't have the jurisdiction to even make that happen, even if we were to prescribe them, specifically.

MR. COSTELLO: If I may. Most of occupational dose in medical institutions result from x-rays. Even the lens of the eye is from x-rays. The amount of dose from byproduct material at medical institutions is pretty near ALARA right now. To me, it's fixing a problem that's not there, at least in the medical arena, anyway.

CHAIRMAN BURNS: Thanks. Dr. Palestro, I was interested in the comments in terms of the

supply of isotopes. I know this is another issue that's gotten the attention of the international community, been providing legal support at NEA for joint declaration on the supply. But as sort of a bottom line given what you showed, I thought it was a very interesting chart in terms of production and use, or production and consumption. Ultimately, it looks like biggest solution in terms of long term is some sort of, you know, isotope producer in the United States, or the ability to do that. Would you agree?

DR. PALESTRO: No, absolutely, because as I had said, it would allow us to control our own destiny, that we're not dependent on outside sources for the molybdenum.

CHAIRMAN BURNS: Yes. At this point as you note, that there are significantly older facilities. And I guess NRU they've extended for another three years. I think originally it was supposed to be, they had announced before, shut down this year and have extended for three years. And I know they have the same issue in terms of the reactors in Europe themselves in terms of it. So, the bottom line, you say there is a lot of work in terms of sort of international cooperation on improving the isotope production of --- I think

it's, in effect, the full cost --- and one of the issues I think internationally has been this issue of full cost recovery, and all.

DR. PALESTRO: Yes.

CHAIRMAN BURNS: But, ultimately, it's about facilities that are able to produce the isotope. Okay. Well, thank you very much. Commissioner Svinicki.

COMMISSIONER SVINICKI: Good morning, and thank you all. I have had the opportunity for a number of years now to participate in the Commission's engagement with your Committee, and I thank all of you and your colleagues who aren't maybe here in the room today for the work that you do.

It's curious to me, I look around the audience today, and I was thinking to myself, I think it's at the end of this month our Commission will hold a meeting on our Fukushima activities, which are very important. I predict that there will be almost no empty seats in the room and, yet, for something that affects all of us, and certainly if you include our close loved ones on a day to day basis, we do not have as many people present. And I hope you don't take it as a sign that there isn't a strong interest, and I'll go beyond that to say

a very essential quality to having the kind of medical and patient advocacy and Agreement State input that the Committee's structure provides to us.

All matters related to nuclear medicine with which I've been involved in time as a Commissioner, I approach as very, very perilous matters because of the fact that there is a real life safety patient outcome element here that I think given the strong defense-in-depth in many other aspects of our regulatory structure are not as keenly present as they are in the medical uses of nuclear technologies.

So, I think that our overall charter to ourselves as the Nuclear Regulatory Commission not to unnecessarily impede, and frustrate, and obstruct the practice of medicine regarding these modalities, and the diagnostic and therapeutic techniques is something that over the course of the years that I've been on the Commission, I think to a person, all members of our Commission have taken very, very seriously. And I think I'll just state that my sense from the NRC Staff is that they have a similar posture on these issues because very consciously we do not attempt to replicate the types of practitioner and patient advocacy expertise that

the Committee provides.

So, I'll just react to a few things. I might have a couple of questions, but since this has been a multi-year dialogue for me, I've developed some decided views on these issues.

Again, I've been reading the medical events reports now for a long time. I read the abnormal occurrence report then that we send forward to the Congress. It is weighted almost exclusively with medical events because we simply do not see the health significant in other aspects of our regulatory framework. We don't see the same thresholds, and so it's interesting to me as a lay person, I read the, you know, one of two paragraph description of these things that again have met the triggers and thresholds to be reported. And then as a lay person I'm reading it, and I say well, it was maybe a dose to the non-treatment site, or something else. It seems so significant to me, and then often I get all the way to the end of the description and what's stated there is the medical assessment is that there is not likely to be an adverse outcome for the patient. And so, if I struggle with that being this much closer to these types of --- of reading this type of reporting, I sometimes think to myself as we forward this on to

the Congress what must they be thinking about the quality of the administration of these various techniques? And I think it's very skewed, and I think it's not accurate, and I regret that. So, when we look at the yttrium-90 microspheres, I appreciate that what we're trying to do there is begin with the end in mind, and not have a whole body of reportable events.

You know, the other aspect is, of course, for a patient. How traumatizing it is for a patient and family to hear that there's something reportable. And then I'm sure they do hear the statement of but we don't assess --- frankly, when there is an adverse outcome expects, it's more likely that it's because we didn't get the treatment to the site where we wanted it, and so I think that's probably remedied in the care going forward. But in any event, great anguish, I think, is created, so there's a real --- there's a global inaccuracy. There is a patient by patient, family by family --- you know, I think a negative consequence that is unneeded, so I think that's something that I appreciate that we continue to try to look at that, and approach that in a more informed way.

Also, the presentation on molybdenum-99 and the tech-99m. You know, I'm reaching a point

where I have been on the fringes of hearing about the impact of this fragile supply chain for so long that's developing beyond an awareness into, I'll confess, a bit of a frustration; particularly, when we look at from the time of the supply interruption. You know, the statistics are compelling in the abstract, and when you think about real patients and real families, and the fact that, you know, maybe --- we had to prioritize, and I'll use this word, ration the delivery of certain things in our country when we are so innovative, so prosperous, have the quality of medical care that we have. I just am frustrated with our national tolerance to be so vulnerable to that kind of supply chain. It is unnecessary. We should view it as intolerable. I know there are financial and other reasons, but I have sat here year by year as I've watched the plans to have U.S. capacity come.

I'm actually not bothered by a foreign dependency, frankly, across our economy, the U.S. You know, we can tolerate being dependent on foreign suppliers, it's true, of rare isotope, you know, the elements and things. And I think as hopefully someday we continue as a nation to explore the promise of radiopharmaceuticals even much more broadly than we have them now, and need to produce

kind of boutique quantities of things, I think having a good global supply chain is perfectly supportable. The problem is that it isn't robust globally, and so I --- you know, at some point you just want to take a deep breath and say I can't believe that we keep allowing this to be this way.

And moly-99, and the tech-99m, and I've had a chance to visit manufacturer, distributors, and so I know about the elution, and I have some very rudimentary understanding of how you milk them, you know, for what you need. Again, we are innovative, in that time of shortfall, I appreciate the slide about all of the innovative ways we came up, but I still don't think it's something that we need to have going on.

I mean, I appreciate that we were innovative about it, but if even one patient was affected by that, my personal view, it's one too many. So, appreciate that someday, some future Commission, some future ACMUI members are going to sit here and be able to talk about this as something that we conquered and put to rest. And I really look forward to that day. I'll be --- if I'm not in the room, I'll be somewhere tuning in cheering that quietly because we need to get on with that.

And then on the input that you provided,

and you I read your written comments on Part 20, which were even more detailed than what was discussed here today, there's a lot of competing things that need to be balanced there. And on the whole, I want to compliment the Committee. I felt that you balanced competing concerns and interests there.

I know that ACMUI, it's difficult to our regulated practitioners of this, and so one could view your input on regulatory changes as being maybe too heavily weighted towards your day to day routine as practitioners. I don't view it that way because of this uniqueness about the delivery of medicine. We heard about recently, it was either in the Washington Post or the New York Times, a long profile critical of FDA, and I have sympathy as fellow regulators for --- I think it was about ALS and some new --- you know, where do they make --- when people are just wanting to kind of manage their illness and prolong their life. How do you balance risk, and making things available? You know, you don't want it to be snake oil about which there's just no good science at all, but on the other hand, if you're a patient or the loved one of a patient your view is I want to weight it towards riskier --- or why can't I make that decision, and why does FDA

get to be the one deciding that? If my loved one could get one more month, he or she wants that, so I appreciate, you know, your sensitivity, because I view your comments as trying to balance that risk, which is different than the power reactor side. And we need to keep our sensitivity tuned very high on that.

I also appreciate your sensitivity to the needs of women working in this field when it came to the embryo and fetus. I think you have a euphemistic statement in there of it's an area of controversy. It's difficult, but there are a lot of competing things to try to balance there. And in instances where we could be more prescriptive or intrusive, I took your comment document to state that what you're trying to do is say what is the benefit to be gained from this? And you're balancing that burden and these other downsides with that. So, I appreciate that.

So, maybe stepping back really generally, one thing that I would be interested in understanding from the Committee, we had an editorial in some trade press a few weeks ago about NRC speaking of the media being critical. In this instance in Energy Daily, there was an opinion piece that NRC's very, very complex regulatory framework

is likely impeding the rollout of new nuclear power-related technologies.

Your Committee provides input to us on I think it's every year or every other year about the effectiveness of the Committee structure, the composition, and things like that. One of the things that you provide feedback on is whether or not you feel the Commission, and I don't know if in answering that question you mean the individual members of the Commission, or the Agency as a whole, has a good understanding of what --- of the practice of nuclear medicine and what it means to deliver that every day, again, through the prism of, you know, patient care and patient outcomes, which is really what's driving you.

If there was something that we could understand better in the --- you know, we can't become you, and we have a lot of other things we're working on, but what would be --- if we had an extra hour each week to get smarter on these issues, if any of you just want to chime in. I'm a little over my time, but I'd like to know since I'm doing wrap-up on the Q&A. What do you think is the keenest gap in terms of what --- the ways you've engaged with NRC or this Commission over the years?

DR. THOMADSEN: I would look at two

issues, and I'm not sure that you can deal with one of them, and that is the issue that came up dealing with the ability to adapt regulations as quickly as needed to deal with the issues that are raised in the community. The changes in regulations have to be transparent, and certainly the NRC works very hard at doing that. You have to get the input from all of the stakeholders, and the NRC works very hard at doing that. I think you do a commendable job at trying to bring in all of the various viewpoints.

The problem is it still takes an awfully long time. The rules for changing regulations do not provide for rapid changes. They probably should not allow changes too rapidly, but there should be some way to address the issues more quickly than what they are now.

The other one, I think in general for the --- from our point of view, our interactions with the NRC Staff have actually been stellar. The NRC Staff that we work with are incredibly sensitive to the issues that we're dealing with, and are trying to deal with them as expeditiously and effectively as possible. That is not always true for all of the people in the field, as we've mentioned. And I think the issue that we were discussing earlier of trying to establish a way to help facilities improve what

they do, particularly when they have the opportunity to see their weaknesses through an event, could certainly be improved and make life less adversarial. That does not usually help the facility in trying to grapple with the issues. They need people who can help them, and they aren't afraid to deal with.

Those would be my two takes on what might be issues that the NRC should consider thinking about.

COMMISSIONER SVINICKI: Thank you. Would anyone else like to offer anything?

MR. COSTELLO: On the rulemaking, have to bring that up again and the germanium. I just call to your attention why I think that should be a simple change. There's a table in Part 20 which gives the quantities of material requiring labeling. There's a table in Part 30 which provides the quantities of material requiring labeling. They're titled exactly the same.

The requirement for decommissioning in Part 30 refers to the table at Part 30. Unfortunately, the table in Part 30 was really not changed after the 2005 Atomic Energy Act revisions, so it doesn't have a quantity for germanium-68. So, you have to use the default quantity. In Part 20,

there is a quantity for germanium-68, and if you could use that quantity there would be no problem with decommissioning. So, you have two regulations, Part 20 and Part 30, with identical tables with different values. One would think that would be a regulatory change that would be easy to make. It almost could be well, we made a mistake. They should be the same. But I don't believe that that, like any regulatory change, can be made inside a year.

COMMISSIONER SVINICKI: Well, I'm over my time, but I'll just close with this. I didn't speak to rulemaking, specifically. Just so you know, this is not unique to the nuclear medicine parts of our regulation. We have over the course of decades now been attempting to embed in our regulations a risk-informed performance-based standard, and what that allows you to do is to have in guidance appropriate, you know, procedures, methodologies, compliance pathways so that the regulations themselves can be robust. But as I sometimes tell the NRC Staff, in my view, the easiest regulation or regulation change to draft is the most prescriptive. To make things robust enough to just be a performance-based or a risk-informed outcome, that's I think the nuanced work. And it's harder to do. We do try to do it. It's a principle espoused,

again, of long standing for NRC, but that allows us as modalities, you know, changes, as techniques evolve, you can simply have it accommodated and not need to make a rule change. We do try on the reactor side, we've been trying to have a technology-neutral framework for a long time, but it's just --- it's hard work. But that's why we embrace that principle, but thank you all, again.

CHAIRMAN BURNS: Thank you, Commissioner. Before we close, anything else?

I want to, again, thank members of the Committee for appearing today and providing very interesting briefing on the various topics related to medical uses of isotopes. I think it's important to hear these views as we look at our regulatory program to hear areas where we may need to focus, and to not have unintended effects in terms of the safe use of radiomedicine. And I, again, also appreciate the participation of all of you, and Ms. Weil in terms of as a Patient Advocate, because it's also important to hear those views and that side of the story, as well.

So, again, thank you, and with that we're adjourned.

(Whereupon, the above-entitled matter went off the record at 11:14 a.m.)